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Clinico-morphologic integration in the surgical repair of atrioventricular septal defect with common atrioventricular junction

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I, Mazyar Kanani, confirm that the work presented in this thesis is my own. Where the information has been derived from other sources, I confirm that this has been indicated in the thesis

Thesis abstract

Atrioventricular septal defect with common atrioventricular junction has been successfully managed surgically for 50 years now. In this time, operative mortality has fallen from 60% to some 2-3% in the modern era. Despite this, almost 10% of these patients develop significant regurgitation of the left atrioventricular valve requiring re-operation within ten years. This figure has not changed in this time. So although patients are surviving more than ever, their ultimate outlook, and potential quality of life has not changed despite major advances in other areas.

In this thesis, I have gone back to first morphologic principles and examined why long-term valve failure has remained disconcertingly stagnant.

The detailed morphology of the trifoliate left atrioventricular valve in atrioventricular septal defects was compared it to its bicuspid normal counterpart, the mitral valve. This latter structure is the "Gold Standard" that the surgically repaired valve should aspire to, with pliable leaflets that are supported with a well-organized subvalvar tension apparatus. Even after bicuspidization of the trifoliate valve in atrioventricular septal defects, this morphologic standard set by the mitral valve is never achieved. One reason for this lies in the so-called Zone of Apposition of the left atrioventricular valve, the area between the left side of the bridging leaflets in the trifoliate valve has both been described as a "cleft" or else a "commissure". This study demonstrates that, morphologically, it is neither, and closure of this Zone in order to bicuspidize the valve does not restore mitral anatomy. Furthermore, this Zone is highly variable in its morphology, and has poor subvalvar support compared to the mitral arrangement.

Finally, the results of repair of atrioventricular septal defects at Great Ormond Street Hospital in the least 10 years were analysed, emphasising the notion that in this modern era, when surgical mortality has been overcome, we should integrate

morphologic understanding wih surgical practice in order to overcome the last hurdle of the defect, and in doing so, secure the long-term quality of life.

Acknowledgments

I wanted to firstly thank my supervisors, Professor Robert H. Anderson, Professor Martin J. Elliott, as well as Mrs. Christine Anderson for their support and generosity during my time at Great Ormond Street. Without them, this body of work would not have existed, yet alone completed. I am also indepted to the British Heart Foundation, who sponsored this work form the beginning. I also wanted to thank Ms. Gemma Price Morgan who helped develop many of the illustrations contained herein. A final mention must be given to Dr. Andrew Cook and Mr. Vi Hue Tran for their kind encouragement and suggestions over the last three years.

Many of the illustrations, especially for Chapter 1 were kindly lent to me by Professor Anderson, from his extensive personal collection. The origin of these images is indicated in the accompanying legend.

For Carl and Robyn Kanani

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Chapter 1: Review of the Literature

Introduction

Following the first successful repair of atrioventricular septal defects at the dawn of modern cardiac surgery, there have been significant advances made in many aspects of overall patient management. In line with improvements in cardiopulmonary bypass, post-operative care and refinement of surgical technique, together with morphologic understanding (Castaneda et. al., 1985 et. al.), there has been a striking reduction in both post-operative mortality and early morbidity. As a counterpoint to this phenomenon, attention has in the last decade focused away from mortality as the single most important outcome measure, and onto the long-term outlook.

Reflecting this increased confidence in the operative management in the last quarter of a century (Rastelli et. al., 1968.) , there has been an evolution in the timing of surgery from a staged approach to an era of complete repair in early infancy (Bender, Jr. et. al., 1982; Castaneda et. al., 1985)

Epidemiology

The prevalence of this defect has been put at 0.19 per 100 live births, accounting for 2.9% of congenital cardiac malformations. In about 60% of these defects, the shunting is confined to the atrial level.

Anatomic considerations

The principle malformation that defines the atrioventricular septal defect lies at the atrioventricular junction. The normal arrangement will be considered first.

The normal atrioventricular junction

The atrioventricular junction is defined as the muscular area that surrounds the orifices of the atrioventricular valves, and marks the point at which the distal margins of the atrial musculature meets the ventricular myocardium. Thus, there are two atrioventricular junctions in the normal heart, one supporting the tricuspid orifice and one supporting the mitral orifice. Although the musculature of the two chambers abut each other over the circumference of this junction, they are nevertheless separable, apart from the area of the muscular axis of atrioventricular conduction - the bundle of His. Wedged in-between the two junctions is the sub-aortic outflow tract, incorporating the in-dwelling aortic valve. Beyond this, anteriorly, is the sub-pulmonary outflow tract mounted on its free-standing infundibulum (Figure 1.1).

Figure 1.1 The normal heart from above with the roof of the atriums removed. There is normal atrioventricular septation, resulting in two separate atrioventricular junctions that serve both sides of the heart. The black star indicates the site of the atrioventricular septum that is bisected by the septal leaflet of the tricuspid valve. The black parenthesis is the position of the atrioventricular muscular sandwich. MV, mitral valve; TV, tricuspid valve; PV, pulmonary valve; MV, mitral valve. Courtesy of Robert H. Anderson

When considering junctional morphology, it is possible to distinguish the points of attachment of the atrioventricular valvar hinges from the points of muscular atrioventricular contiguity. At the right atrioventricular junction, where the hinges of the tricuspid valve are anchored by muscle throughout, these two areas are essentially the same, apart from the short length where the septal leaflet of the valve crosses the

membranous septum. In doing so, it divides the membranous septum into atrioventricular and interventricular components (Figure 1.2).

Figure 1.2 A diagrammatic representation of the normally septated heart showing the relationship between the subaortic outflow tract and the atrioventricular septum and sandwich. Note how the subaortic outflow tract is wedged between the two atrioventricular junctions. Courtesy of Robert H. Anderson

This disparity between the muscular atrioventricular junction and the valvar annulus is most clearly seen at the mitral valve, where the fibrous tissue of the aorto-mitral fibrous continuity supports one-third of the annulus (Figure 1.3).

Figure 1.3 A photographic equivalent of Figure 2 The coronary sinus and circumflex branch of the left coronary artery skirt around the parietal left atrioventricular junction. Courtesy of Robert H. Anderson

The atrioventricular septum and sandwich

When observed in the four-chamber view, the tricuspid annulus is seen to lie at a more apical position than to its mitral counterpart. Consequently, in the region immediately caudal and posterior to the area where the septal leaflet traverses the membranous septum, the muscular atrial septum overlaps the crest of the ventricular septum. This area between the offset hinges of the atrioventricular valves has previously been called the muscular atrioventricular septum (Becker et. al., 1982), but is, in fact none other than an extension of the fibro-fatty tissue of the posteroinferior atrioventricular groove (Figure 1.4).

Figure 1.4 A specimen of the normal heart taken in four-chamber section. The normal off-setting of the hinge points of the mitral and tricuspid valves gives rise to the atrioventricular septum (marked by the black star). RA, right atrium; LA, left atrium; IVS, interventricular septum. Courtesy of Robert H. Anderson

By rights, therefore, atrioventricular septum should, be reserved for the atrioventricualr component of the fibrous membranous septum. It is the absence of these two components – the fibrous membranous septum and the fibro-fatty muscular sandwich, that define hearts with atrioventricular septal defects, more than any other anatomic feature.

The common atrioventricular junction in atrioventricular septal defects

The common atrioventricular junction is the fundamental feature that sets the atrioventricular septal defect apart from the normal heart (Figure 1.5).

Figure 1.5 Left panel: a schematic representation of the heart with atrioventricular septal defect with common atrioventricular junction, looking from the atrial aspect. The roof of the atriums have been removed. There is a common annulus that serves both ventricles, being surrounded by a common atrioventricular valve, with five leaflets. The black arrow indicates the position of the zone of apposition between the left sides of the superior and inferior bridging leaflets that has previously been called a "cleft". Right panel: a photographic equivalent of the left panel. Courtesy of Robert H. Anderson

It occurs, irrespective of the number of valvar orifices to the defect, and is seen even in the absence of septal deficiency. All other morphologic features seen in this defect arise as a direct consequence of this singular arrangement of the junctional structures. Other morphologic markers can be considered under the following subheadings:

- Leaflets arrangement
- Septal deficiency
- The ventricular mass
- The subaortic outflow tract
- The conduction axis

Leaflet arrangement and the subvalvar apparatus

The oval-shaped common atrioventricular junction in atrioventricular septal defects surrounds an orifice that is guarded by a valve that usually possesses five leaflets. There is some variability in this arrangement, depending on the permutation of leaflet fusion. Variable fusion may result in separate right and left orifices, or may produce any number of accessory orifices depending on the location and extent of fusion.

Lying across the crest of the ventricular septum, to a variable extent, are the superior and inferior bridging leaflets (SBL, IBL). These were previously known as the anterior and posterior bridging leaflets, respectively, and have no counterparts in the normally septated heart (Figure 1.5 – left panel).

Adjacent to the SBL over the orifice of the right ventricle is the antero-superior leaflet (ASL) that is analogous to its tricuspid counterpart. Supported by the parietal margins of the common junction on both sides are the right and left mural leaflets. The right mural leaflet lies against the ASL and IBL, the left leaflet lies in apposition with the SBL and IBL.

The subvalvar apparatus is similarly abnormal, most conspicuously in the arrangement of the papillary muscles. The two left-sided papillary muscles normally lie

obliquely, assuming antero-lateral and postero-medial attitudes. In AVSD, these two muscles are located in the same vertical plane, being positioned superiorly and inferiorly, hence their names (Figure 1.6).

Figure 1.6 Diagrams of the atrioventricular arrangement in the normal heart (a) and heart with deficient atrioventricular septation (b) (Abbruzzese et. al., 1990), taken from Ebels et. al. 2002 View is from the ventricles below. This not only shows the abnormal atrioventricular arrangement in atrioventricular septal defects, but also the abnormal leaflet and papillary muscle positioning. Ao, aortic orifice; T, tricuspid orifice; M, mitral orifice; C, common orifice; RV, right ventricle; LV, left ventricle; MPM, medial papillary muscle; APM, anterior papillary muscle; IPM, inferior papillary muscle; ALPM, antero-lateral papillary muscle; PMPM, postero-medial papillary muscle; SPM, superior papillary muscle. Courtesy of Robert H. Anderson

The superior muscle supports the zone of appostion at the SBL-mural leaflet interface, and the inferior muscle, the zone of apposition between the IBL and mural leaflets. Unlike the right side, the position of these left-sided muscles are consistent. However, they may be found in clusters, as in the so-called parachute arrangement, where the cords from all leaflets converge onto only one papillary muscle (Figure 1.7).

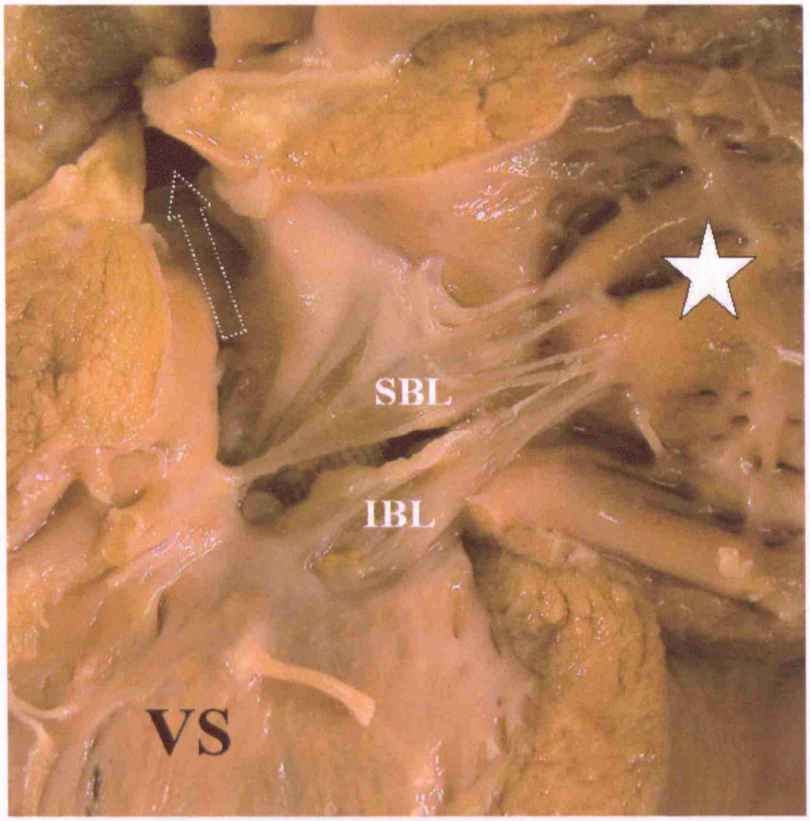

Figure 1.7 A specimen of atrioventricular septal defect looking from the left ventricular aspect. There is a solitary papillary muscle arrangement, where the superior (SBL) and inferior (IBL) bridging leaflets converge to a single papillary muscle (white star). The white broken arrow indicates the position of the subaortic outflow tract. VS, ventricular septum

Rastelli classification and right ventricular papillary muscles

The papillary muscle arrangement of the right side depends on the degree of bridging of the SBL across the ventricular septal defect. This forms the basis for the Rastelli classification (Rastelli et. al., 1966; Rastelli et. al., 1968).

When there is minimal bridging of the SBL into the left ventricle, or Rastelli class A, the edge of the leaflet is tethered to the crest of the septum (Figure 1.8 – left panel). Here, the ventricular septum is analogous to a papillary muscle, supporting the Zone of Apposition between the SBL and IBL. In this situation, the ASL of the right atrioventricular valve is well developed and morphologically similar to its tricuspid counterpart. At operation, this arrangement gives the appearance of the SBL being divided over the septum (Figure 1.9a).

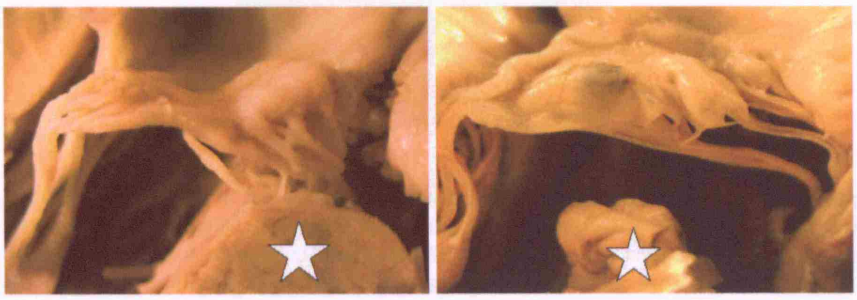

Figure 1.8 Specimens showing variations in the degree of bridging of the superior bridging leaflets, which forms the basis of the Rastelli classification. This is a four-chamber orientation, and the white stars indicate the position of the ventricular septum. Left hand panel – the so-called Rastelli Type A arrangement where the SBL is minimally bridged, and bound to the crest of the ventricular septum. Right hand panel- the Type C arrangement where the SBL bridges the septum to the greatest extent and is floats freely

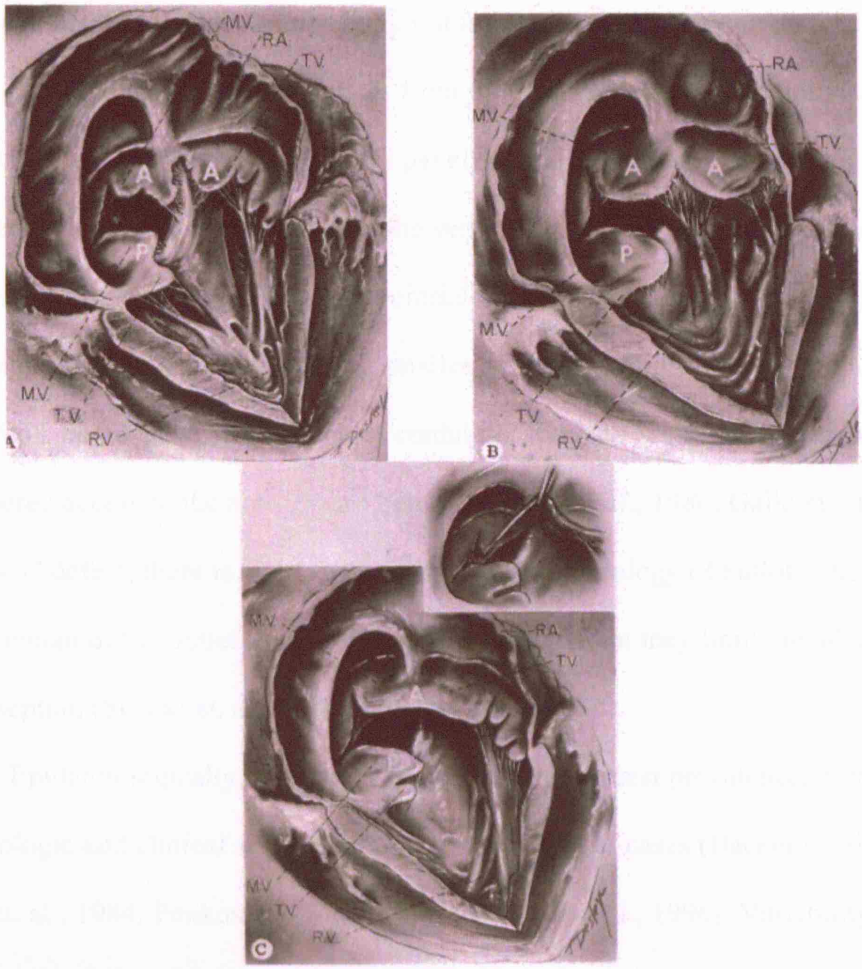

Figure 1.9 Figures taken from Rastelli's study on the arrangement of the superior bridging leaflet in atrioventricular septal defects (a to c). In the type A, the superior bridging leaflet is minimally bridged, with most of the leaflet confined to the left ventricle, and tethered to the septum. In the Type B, the degree of bridging is greater, with its right ventricular attachment being to an anomalous papillary muscle. In the Type C, the leaflet is maximally bridged, being free-floating (box of panel c) and attached onto the medial papillary muscle of the right ventricle with the antero-superior leaflet

Subsequent anatomic observation, determined that this "division" of the SBL over the septum merely represents the zone of apposition between the SBL and well-formed ASL in the class A defect, and that in all classes of the defect, the SBL is undivided over the ventricular septum (Anderson et. al., 1985; Penkoske et. al., 1985; Ugarte et. al., 1976). In the class B defect, the SBL extends further into the right ventricle, with further reduction in the size of the ASL. It is usually unattached to the

ventricular septum, but at its right margin it is supported solely by an anomalous right ventricular papillary muscle that arises from the septomarginal trabeculation. In the so-called type C defect (Figure 1.8 – right panel), the SBL extends even further into the right ventricle and floats freely above the ventricular septum, extending from the anterior papillary muscle of the right ventricle to the superior papillary muscle of the left ventricle. The ASL is necessarily smaller, accommodating the greater encroachment of the SBL into the right side. Lack of cordal attachments to the septum ensures unhindered access to the aortic valve beneath (Ebels et. al., 1986; Gallo et. al., 1991). In the type C defect, there is a high association with the tetralogy of Fallot, when rightward displacement of the outlet septum during the development may limit cordal attachment to the septum (Suzuki et. al., 1998; Uretzky et. al., 1984).

Epidemiologically, the type A defect has the greatest prevalence, both in morphologic and clinical series, ranging from 50-75% of cases (Backer et. al., 1995; Bove et. al., 1984; Penkoske et. al., 1985; Redmond et. al., 1996). Variability in the degree of bridging of the SBL may also be seen in cases of AVSD with separate orifices, or the so-called "partial defect", where minimal bridging of the SBL is the most common pattern seen (Penkoske et. al., 1985)

The nature of the Zone of Apposition: "cleft" or "commissure"?

The area in between left sides of the bridging leaflets has been the subject of much historical controversy. The principle question is whether it represents a cleft, as in the so-called isolated cleft of the anterior leaflet of the mitral (McGoon et. al., 1981), or whether it is the commissure between the leaflets of a left atrioventricular valve. A commissure is the functional division between the leaflets of a valve that is supported by a fan-shaped tendinous cord atop a papillary muscle. A cleft is defined as a space or

opening made by splitting the anterior leaflet (Van Praagh et. al., 2003). Given these definitions, this space between the bridging leaflets, may be best thought of as septal commissure in a tri-foliate leaflet atrioventricular valve.

Morphology of the atrial and ventricular septal defects

Although septal deficiency is almost uniformally seen in hearts with this defect, the pattern of blood flow between the chambers is largely determined by the cordal and leaflet anatomy.

The ventricular septum in AVSD is "scooped", with a gentle curve extending from the crux of the heart to the left ventricular outflow tract (Figure 1.10).

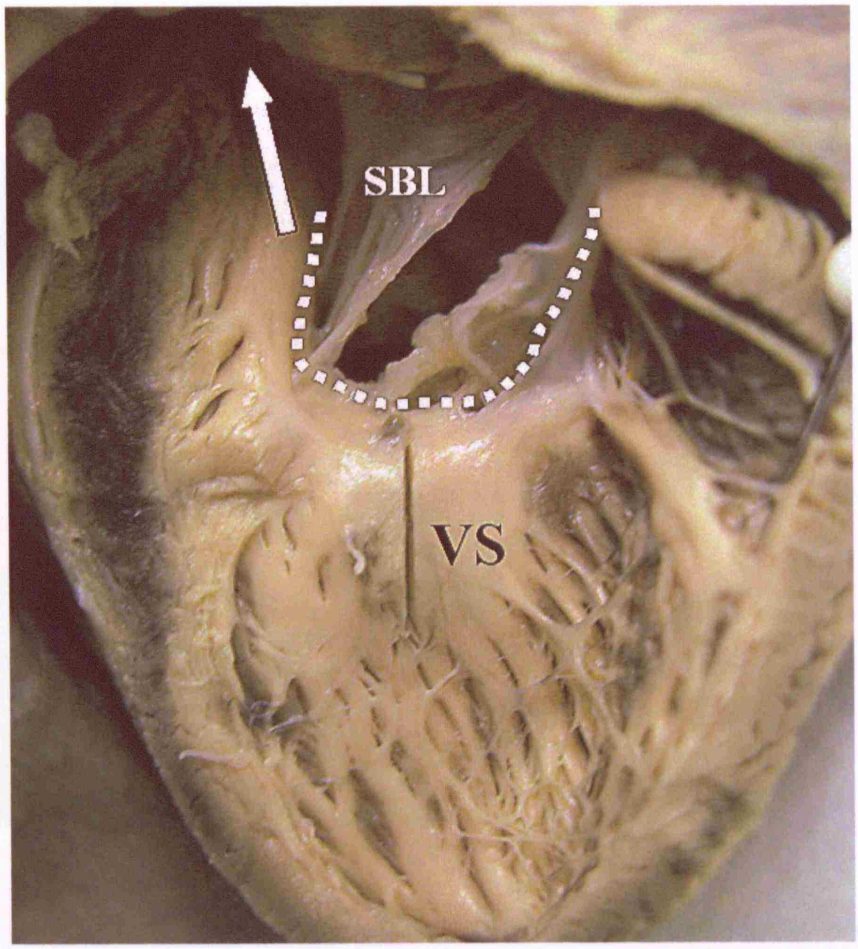

Figure 1.10 A specimen of atrioventricular septal defect looking from the left ventricle in long-axis section. The scooped out appearance of the crest of the ventricular septum (VS) has been marked by the white line. The white arrow points to the narrowed subaortic outflow tract.

The depth of the scoop, and the resulting deficiency is very variable, being more extensive in hearts with common orifices (Ebels et. al., 1990; Gutgesell et. al., 1986; Penkoske et. al., 1985).

Above the plane of the annulus is the so-called ostium primum defect (Figure 11), which in some instances may be obliterated through attachments of the leaflets to

its edge, giving rise to obligatory ventricular shunting. If combined with a secundum atrial septal defect, it may produce a common atrium.

Figure 1.11 Specimen of atrioventricular septal defect looking from the left ventricle showing the relationships between the atrial septal defect (ASD), ventricular septal defects and bridging leaflets (SBL and IBL). The white line shows the characteristically crescenteric shape to the deficient inferior rim of the atrial septum, forming the so-called ostium primum component. Courtesy of Robert H. Anderson

Common vs separate orifices

There are two varieties of atrioventricular septal defect, depending on the level of intra-cardiac shunting caused by the pattern of leaflet fusion. However, when the leaflets are stripped from both variations, their junctional morphology is identical (Becker et. al., 1982).

In the defect with separate orifices, also known as the partial AVSD, there is a tongue of leaflet connecting the bridging leaflets over the ventricular septal crest.

Therefore, the septal communication beneath the leaflets is obliterated, limiting shunting to the atrial level (Figures 1.12 and 1.13).

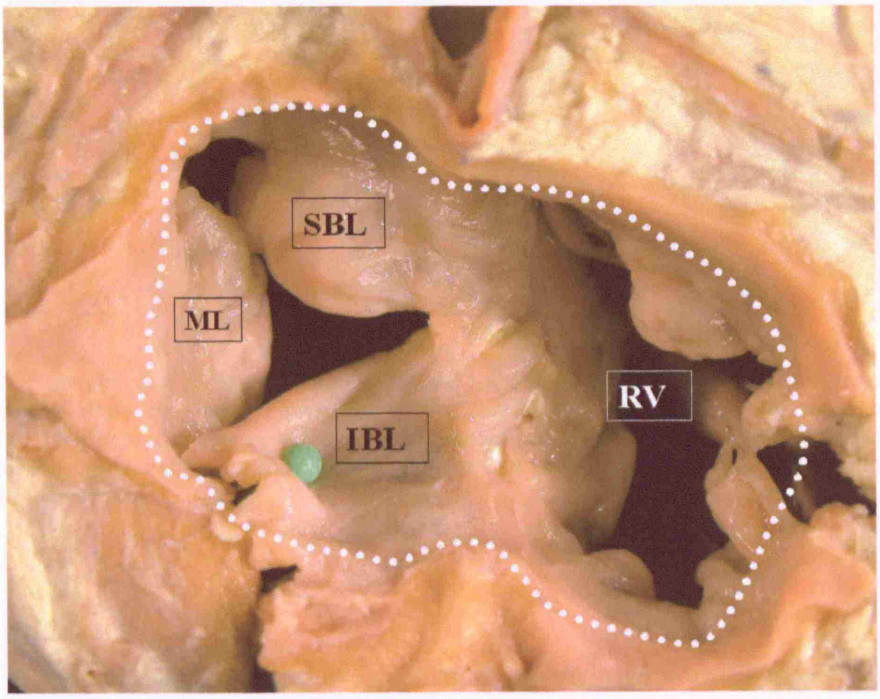

Figure 1.12 A specimen of atrioventricular septal defect with common atrioventricular junction (encircled by the white line), but with separate orifices. Their orifices are divided by a connecting tongue of tissue between the SBL and IBL, which is also bound to the crest of the ventricular septal defect. This closes off the ventricular communication. ML, mural leaflet of the left atrioventricular orifice.

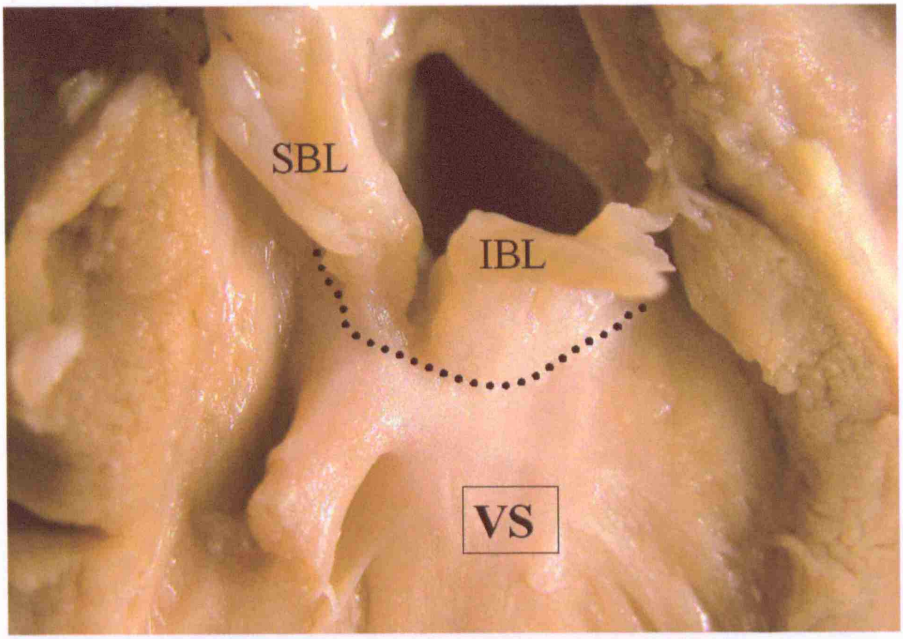

Figure 1.13 Specimen of atrioventricular septal defect with separate orifices, looking from the left ventricle. The white line shows the position of the crest of the ventricular septum, which is bound to the bridging leaflets, thus closing off any ventricular communication. Note how the zone of apposition has a three dimensional configuration, in that is rises up from the septum before continuing forward.

Although this fusion results in separate atrioventricular orifices, the connecting tongue is not a continuation of the common annulus across the septum. The morphologic extent of this tongue again shows variability. In some instances, the bridging leaflets are fused with each other, but multiple intercordal spaces beneath the leaflets leave the potential for interventricular shunting (Figure 1.14).

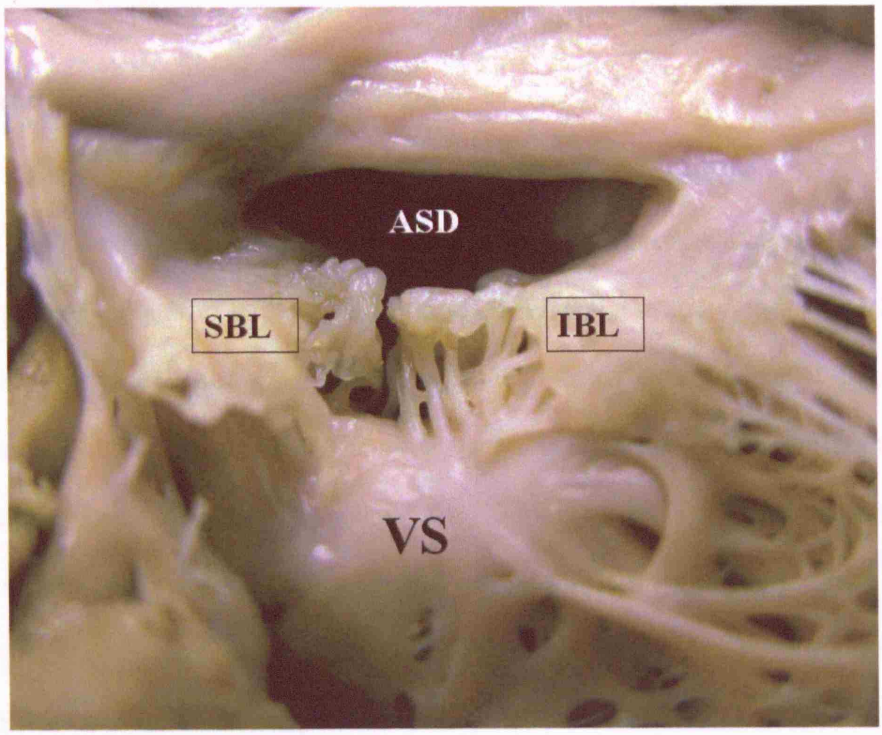

Figure 1.14 Specimen of atrioventricular septal defect, looking from the left ventricle. this is a defect with a common orifice, but there are multiple small intercordal communications between the ventricles. This has previously been called the "intermediate" or "transitional" defect.

Hearts exhibiting this latter phenomenon have been termed the "intermediate" or "transitional" AVSD, emphasising separate orifices in the context of persisting ventricular shunting, as if it was embryologically a transitional form between two extremes. We believe that this term is misleading and loses sight of the fact that defining feature of hearts with this defect is deficiency of atrioventricular septation, and not leaflet morphology. As such, septation may be deficient or otherwise, with no intermediate arrangement (Ebels et. al., 1991). Despite the clinically more benign course of the defect with separate orifices, there is a greater prevalence of subaortic obstruction, papillary muscle anomalies and leaflet dyspalsia (Penkoske et. al., 1985). Nevertheless, the association with other complex malformations is more common in hearts with a common orifice.

Ventricular morphology and balance

In the normal heart, the inlet to outlet ratio is the same (Figure 1.15 – left panel). This is also seen in hearts with perimembranous ventricular septal defects, and hearts with an isolated "cleft" in the anterior leaflet of the mitral valve, which have all been previously described as the "formes fruste" of atrioventricular septal defect (Di Segni et. al., 1983). In the latter, the outlet length is significantly longer than the inlet, and can be appreciated from the "swan-neck" deformity of the subaortic outflow tract (Figure 1.15 – right panel). This has been explained in terms of a shorter inlet (Blieden et. al., 1974) or a longer outlet (Van Groningen et. al., 1990). Theses ratios are the same in AVSD with common and separate orifices.

Figure 1.15 Left hand panel, showing the comparable inlet and outlet dimensions of the normal heart. Right hand panel – shows the inlet dimension of the heart with the atrioventricular septal defect is much less that the elongated outlet. This accounts for the scooping of the ventricular septum. Courtesy of Robert H. Anderson

The diameters of the inlets of both ventricles as well as the volumes of the ventricles are the same, or balanced, with the atrial and ventricular septums being in line. In the era of the two-staged repair, a reduction in the volume of the right ventricle was occasionally observed after pulmonary trunk banding owing to hypertrophy of the trabecular layer of the myocardium. Aside from this special situation, left dominance may occur with hypoplasia of the right ventricular and pulmonary arterial components, typically in association with malalignment of the atrial and ventricular septums. This leads to the most extreme case of double inlet left ventricle with common atrioventricular valve (Smallhorn et. al., 1981). In the case of right dominance, there is usually hypoplasia of the left ventricular and aortic structures with normal alignment of the atrial and ventricular structures (Drinkwater et. al., 1997).

The subaortic outflow tract and subaortic stenosis

Although the subaortic outflow tract is narrower (Chang et. al., 1987) and longer (Ebels et. al., 1986) than normal, as seen on angiography, obstruction is surprisingly uncommon in the clinical setting (Piccoli et. al., 1982) (Figure 1.15 – right panel).

The principle source of obstruction comes from the anterior and un-wedged position of the subaortic ouflow tract, which is a direct product of failure of atrioventricular septation. This exaggeration of the sub-aortic outflow tract is also more pronounced in hearts with the Rastelli type A leaflet morphology, where the SBL is tethered to the crest of the ventricular septum, narrowing the outflow tract even further. This also explains why obstruction is more frequent in the setting of separate orifices.

Additionally, the superior papillary muscle, or an anomalous portion of it may extend into the subaortic outflow tract (Figure 1.16), or there may be a prominent anterolateral trabecular muscle bundle. Similarly, there may be accessory tissue tags or cordal attachments hanging from the SBL, further obstructing the path.

Such hearts may also become obstructed through mechanisms that affect normally septated hearts, such as fibrous sub-aortic shelves.

There may also be a further, dynamic component to the potential for obstruction in these hearts. The elongated outflow tract is a muscular tube that constricts during systole, heard as a persisting systolic murmur in the absence of clinically significant left atrioventricular valve regurgitation (Ebels et. al., 1984).

Obstruction is also well recognized in the post-operative setting, such as after left atrioventricular valvar replacement, where it accounts partly for the high mortality in these cases.

Figure 1.16 A specimen of atrioventricular septal defect, looking from the left ventricle towards the left ventricular outflow tract (white star). Thus, the underside of the superior bridging leaflet (SBL) is seen. The white line indicates the margins of the superior papillary muscle (SPM) that extends up the left ventricular outflow tract, causing further narrowing of the already elongated outflow tract

The morphology of the atrioventricular conduction axis

The displacement of the conduction axis is the direct result of deficient septation with absence of the central fibrous body that normally marks the point at which the atrioventricular node continues as the atrioventricular bundle. There is some variability among hearts with the atrioventricular septal defect, depending of the alignment of the atrial and ventricular septums. Thus, the nodal triangle is displaced posteriorly and inferiorly, and lies in the posterior right atrial wall, between the orifice of the coronary sinus and the crux of the heart.

From this position, the bundle of His passes to the crest of the ventricular septum through the crux, which is the first point of contact of the atrial and ventricular musculature. It runs along the crest of the septum under the cover of the IBL, giving off left bundle branches. At about the mid-point of the ventricular septum, it becomes the right bundle branch that descends to the medial papillary muscle of the right ventricle (Figure 1.17). Thus, at operation, the greatest danger is at the time of securing the atrial septal patch, when the node is approached at the crux.

Figure 1.17. The position of the conduction axis in atrioventricular septal defects. The view is from the opened right ventricle. The margins of the triangle of Koch is indicated, the blue star indicates where one would normally expect to locate the atrioventricular node i.e. at the apex of the triangle. However, in the defect, the node has been displaced to the area between the coronary sinus and the crux of the heart (red star). From here the conduction axis runs along the proximal part of the ventricular crest. Courtesy of Robert H. Anderson

Pathophysiology

The volume and pressure loading on the heart depends on the level and degree of shunting. Shunting may occur at the atrial level, ventricular level, or across both chambers via the Zone of Apposition. This, in turn, will be determined by the size of the septal defect(s) and the competence of the atrioventricular valves.

With separate orifices

There will be a left to right shunt at atrial level, producing right heart volume overload. In the context of a competent left atrioventricular valve (LAVV), the haemodynamic consequence of this is similar to a defect in the oval fossa (Figure 1.18).

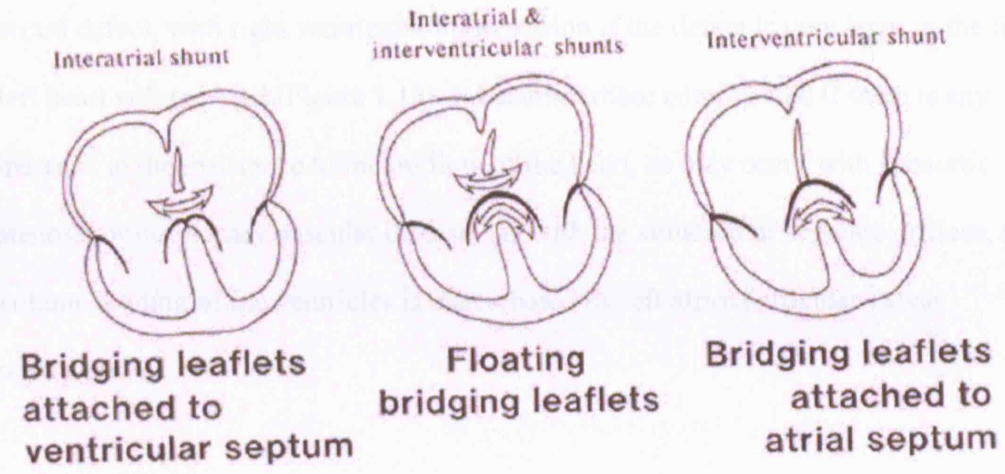

Figure 1.18 The potential for shunting across the atrial and ventricular septal defects in atrioventricular septal defects will be determined by the pattern of leaflet fusion to the leading edge of the septums. Reproduced from Ebels et al. 1990

However, the influence of the LAVV must be considered. Even a mild or moderate degree of regurgitation may be enough to increase substantially the volume overload. Similarly, regurgitation through the valve may shunt blood from left ventricle

to right atrium. This phenomenon is limited to heart with atrioventricular septal defects, with or without a common atrioventricular junction. This is an obligatory shunt, being a direct consequence of the anatomic defect in the left atrioventricular valve, and independent of the pulmonary vascular resistance.

In the context of the common atrium, which occurs with a concurrent defect in the oval fossa, or isomerism of the atrial appendages, there is free mixing of systemic and pulmonary venous blood. This is especially true with isomerism, where there may be abnormalities of the systemic venous return.

With common orifices

In the simplest case, the shunting is from left to right, similar to a ventricular septal defect, with right ventricular hypertension if the defect is very large in the face of left heart volume load (Figure 1.18). It becomes more complicated if there is any increase in the resistance to the outflow of the heart, as may occur with subaortic stenosis or pulmonary vascular disease. As with the situation of separate orifices, the volume loading of the ventricles is exacerbated by left atrioventricular valvar regurgitation.

Pre-operative left atrioventricular valvar regurgitation

The reasons for left atrioventricular valvar incompetence have not been fully elucidated. As with the normal atrioventricular valves, competence is a product of the interplay between valvar and subvalvar factors. These include the contraction of the annulus during the cardiac cycle, successful coaptation of the leaflet edges, support from the tendinous cords along with normal papillary muscle function. Although these influences in this abnormal arrangement has yet to be elucidated, it is known that most of the regurgitation takes place at the Zone of Apposition, getting worse with progressive leaflet dysplasia, and annular dilatation. This is the principle reason why repair should, almost always, include attention to this zone (Castaneda et. al., 1985).

Some 40% of patients exhibit moderate to severe pre-operative regurgitation (Bando et. al., 1995; Studer et. al., 1982), but this may reflect the age at presentation in the older data and variability in the standards used to judge regurgitation. Other series have put the prevalence of moderate to severe regurgitation with common orifices at 15-20% (Abbruzzese et. al., 1983; Chin et. al., 1982; Weintraub et. al., 1990).

However, despite these concerns, pre-operative regurgitation has seldom been found to be a risk factor for early post-operative regurgitation (Bando et. al., 1995; Kirklin et. al., 1986; Studer et. al., 1982), and even patients with severe regurgitation may be repaired successfully (McGrath et. al., 1987; Tweddell et. al., 1996; Weintraub et. al., 1990) .

The influence of Trisomy 21

Congenital heart disease has an overall prevalence of 29% in those with Trisomy 21, with some 75-80% of those with atrioventricular septal defects being affected by trisomy 21 (Baird et. al., 1987). Three principle issues relate to the impact of this condition on the management of this defect.

The first involves the morphologic differences seen in the heart with trisomy 21. There is a higher prevalence of atrioventricular septal defect with a common orifice in Trisomy 21, especially the Rastelli A variant. Also, the entity previously known as the intermediate, or transient, variant that has a restrictive ventricular component, is more common (Marino, 1992). Some have also stressed that the morphology found with Trisomy 21is probably more favourable to repair, with a consequently lower incidence of reoperation for valvar regurgitation (Michielon et. al., 1997; Studer et. al., 1982). However, the most striking difference found lies in the increased incidence of left ventricular outflow obstruction (De Biase et. al., 1986), irrespective of the number of valvar orifices.

Another issue relates to the implications of pulmonary vascular disease on the feasibility and timing of surgery. The impact of pulmonary vascular disease on the repair of ventricular septal defects has been known since the 1950's. Since then, attention has focused on surgery before irreversible vascular changes occur, especially for those with trisomy 21 where these changes occur earlier and progress more quickly (Chi et. al., 1975; Clapp et. al., 1990). More intriguing is the impact of this finding on the policy towards the complete repair. The debate as to whether they should even be repaired, let alone its timing had raged for some years, but came into sharp focus in the mid 1980's with a challenge to the view that children with trisomy 21 should undergo surgery in the same manner as other children with AVSD (Bull et. al., 1985). It was

held that the overall surgical mortality was in the order of 20%, but that the life expectancy of those children with trisomy 21 who had received medical therapy alone was 80% at 15 years, with good quality of life (Figure 1.19). This view has been rebuffed in the modern era, since the contentions and arguments of the Bull paper were based on results stretching back to 1970, when early operative mortality was greater than 20%. Presently, surgical mortality has fallen to a level that negates the view that surgery should be withheld in trisomy 21 on the basis of early operative mortality data alone.

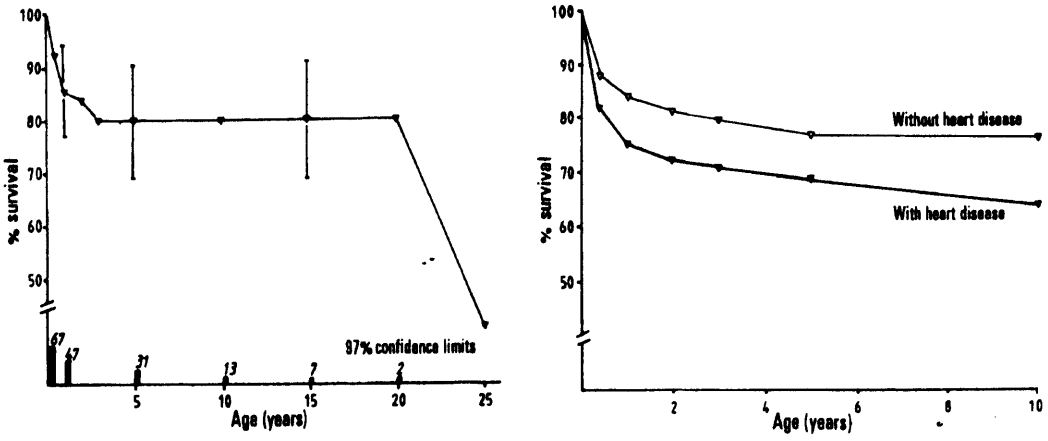

Figure 1.19 Kaplen-Meier survival graphs from Bull et al. 1985. The left hand graph is the actuarial survival of 67 patients with Trisomy 21 and AVSD manged medically. The right hand survival curve shows the actuarial survival for the first 10-years of life in children with trisomy 21 with and without congenital heart disease. The latter data was based on data from 1955 to 1966.

Clinical Features

The presentation and clinical findings of those with atrioventricular septal defects are determined by several factors, aside from the impact of any concurrent cardiac malformations. Notably, these are the level of shunt, and the competence of the left atrioventricular valve.

In the presence of isolated atrial shunting and minimal valvar regurgitation, the presentation is often delayed, akin to a defect in the oval fossa. The findings may be made incidentally, or suspicion raised by recurrent chest infections and reduced exercise tolerance.

With a common orifice, and shunting at both levels, presentation is usually in infancy, with cardiac failure. The child is sweaty, short of breath on feeding, and fails to thrive. These are compounded if there is severe left atrioventricular valvar regurgitation. On examination, the child is undernourished, breathless, and tachycardic with hepatomegaly. There is a hyperactive preacordium with a systolic thrill, and a pansystolic murmur of variable grade.

Investigations

Chest radiography

There is an increase in the cardiothoracic ratio due to cardiomegaly. Even in the absence of severe intracardiac shunting, the heart is enlarged if the atrioventricular valves are severely regurgitant. The pulmonary trunk is similarly engorged, with prominence of the pulmonary vascular markings.

In the presence of pulmonary hypertension, the heart may not be greatly enlarged, but the pulmonary trunk may still be engorged, with "pruning" of the markings of the vascular tree.

Angiocardiography

Although superseded by echocardiography, (Lipshultz et. al., 1988) it is presently reserved for those patients with complex defects where the intracardiac shunt must be calculated, and when operability needs to be determined in the face of raised pulmonary vascular resistance. Information provided includes the anatomy, degree of atrioventricular valvar regurgitation and quantification of shunt.

The diagnostic hallmark is the "gooseneck" appearance of the left ventricular outflow tract in the antero-posterior projection (Blieden et. al., 1974) (Figure 1.20).

Figure 1.20 An antero-posterior angiocardiographic projection of the heart in atrioventricular septal defect with common atrioventricular junction. The left ventricular outflow tract is elongated as a "goose-neck" (outlined) since it lies in an un-wedged position anterior to the common atrioventricular junction. Courtesy of Robert H. Anderson

Echocardiography

This has superseded all other modalities as the pre (Cabrera et. al., 1990; Lange et. al., 2000), intra (Ungerleider et. al., 1989; Zellers et. al., 1994) (Canter et. al., 1997) and post-operative (Kececioglu et. al., 1997) investigation of choice. Doppler interrogation reveals intracardiac shunting, atrioventricular valve function, left ventricular outflow patency and the determination of the pulmonary vascular pressures. It has also, in recent years, been applied for prenatal diagnosis (Fesslova et. al., 2002).

There are a number of anatomic hallmarks. On the four-chamber view, the common atrioventricular junction causes loss of the normal offsetting of the atrioventricular valves (Figure 1.21). Furthermore, the relationship of the leaflets to the crest of the ventricular septum can be appreciated on this view (Figure 1.21 – right hand panel).

On the long axis section, the "goose-neck" deformity of the left ventricular outflow tract is also visible; and on the short-axis, the common atrioventricular valve annulus is seen (Figure 1.22). With separate right and left orifices, the trifoliate left atrioventricular valve is seen on short-axis with its characteristic orientation of the leaflets.

On-table echocardiography in the operating room is often used following repair in order to aid intra-cardiac de-airing, and determine ventricular function, the competence of the valvar repair and the presence of any residual intracardiac shunt. In a child of over 3.5 kg, this may be performed through the trans-oesophageal route and in smaller patients using an epi-cardial probe.

Figure 1.21 Two-dimensional transthoracic echocardiogram of the heart with atrioventricular septal defect in four-chamber view, taken in diastole (left hand panel) and systole (right hand panel). Note the tethering of the bridging leaflets to the crest of ventricular septum in systole. RA, right atium; LA, left atrium. Courtesy of Robert Yates

Figure 1.22 The same heart as figure 1.23, in short axis orientation showing the characteristic shape of the common atrioventricular junction (outlined). Courtesy of Robert Yates

The size of the ventricular septal defect is variable, often being larger beneath the superior bridging leaflet. There will also be variable cordal tethering to its crest. This septal tethering is greatest beneath the inferior bridging leaflet, as seen on the four-chamber section. It is therefore important to look for subtle ventricular shunting in the intercordal spaces with colour flow Doppler interrogation. Thus, because of this cordal obstruction, the degree of interventricular shunting is greatest with a free-floating superior bridging leaflet. These so-called Type C defects also occur in association with deviation of the outlet septum, such as the tetralogy of Fallot and double outlet right ventricle (Suzuki et. al., 1998).

The sizes of the ventricle may also be assessed with reference to whether a bi-ventricular repair is possible, and if there is any concurrent outflow tract obstruction. A small left ventricle may be seen in the setting of coarctation of the aorta, and small right ventricular cavity may be seen following the muscular hypertrophy that occurs after pulmonary trunk banding.

Natural History

Without surgical intervention, the natural course will be determined by a number of factors. Principally, the level and degree of the intracardiac shunting, the pulmonary vascular resistance and the competence of left atrioventricular valve. It also follows that these factors will impact the timing of surgical intervention, and subsequent outcome.

For defects with separate orifices, in the absence of significant left atrioventricular valvar regurgitation, as discussed previously, the natural history will be similar to a defect in the oval fossa. Therefore, up to 15% will develop pulmonary hypertension by adulthood, and symptomatic deterioration may coincide with the development of atrial fibrillation (Somerville, 1965).

As predicted, the clinical course for the defect with a common orifice is more pernicious, with early deterioration from pulmonary hypertension, cardiac failure or respiratory infections. It has been estimated that up to 80% of patients who did not undergo operation died by the age of 2 years (Berger et. al., 1979).

Surgical Management

The historical perspective

There are two pivotal historical events that transformed the surgical repair of atrioventricular septal defects. The first, and most conspicuous was the advent of cardiopulmonary bypass, but this could not have achieved its success without the other crucial event, mapping the conduction tissue by Lev (Lev, 1958). Up to then, repair was hazardous, even in the best hands. In 1954, Kirklin and associates successfully closed a defect with sparate orifices using the atrial well of Gross. By 1955 defects were being

closed under cardiopulmonary bypass using the DeBakey roller pump and wire-mesh screen oxygenator (Kirklin et. al., 1955).

Lillehei and associates performed the first repair of the so-called complete defect in 1954 by suturing the inferior rim of the atrial septum directly to the crest of the ventricular septum. Unsurprisingly, this often caused complete heart block, worsening valvar regurgitation and sub-aortic stenosis. This led to the introduction of the single patch technique in 1962 (Maloney, Jr. et. al., 1962) as a way of overcoming early mortality. Over the last four decades, results have continued to improve, owing to better surgical techniques; more refined bypass circuits, and improved post-operative care together with the use of permanent pacemaker systems.

One vs. two-stage repair

In the modern era, attention has shifted from a two-stage repair, involving initial pulmonary artery banding, to complete primary repair in infancy. What factors have brought about this change of strategy? There are two reasons for this. Firstly, there is greater understanding of the morphology, as mentioned. This also advanced the appreciation of the abnormal pathophysiology. Thus, it was recognised quickly that banding was often ineffective in alleviating heart failure in the presence of severe left atrioventricular valvar incompetence (Hunt et. al., 1971). Overall, the mortality associated with banding approached 50% (Hunt et. al., 1971; Newfeld et. al., 1976; Stark et. al., 1969). Faced with these concerns, complete repair before the age of two years was called for, bringing the timing of intervention into line with that of simple ventricular septal defects (Mair et. al., 1977). By the late 1970's early primary repair was the norm (Kirklin et. al., 1979), some even having practiced this routinely in the earlier part of that decade (Mair et. al., 1977).

Presently, initial banding is reserved for complex defects, such as multiple ventricular septal defects, concurrent sepsis, and in some cases of the so-called unbalanced atrioventricular septal defects, when feasibility of biventricular repair can be made at a later date (Bando et. al., 1995; Capouya et. al., 1992; Reddy et. al., 1998; Redmond et. al., 1996).

Timing of repair

Hand in hand with primary repair is a decline in the age at operation. Independent of age, the timing will also be determined by other factors, such as the pulmonary vascular resistance, size of the intracardiac shunt and the degree of left atrioventricular valvar regurgitation. Aside from the protective effects on the pulmonary circulation (Bando et. al., 1995), earlier age at repair may confer benefits to the competence of the left atrioventricular valve. Chronic valvar regurgitation and volume overload lead to progressive annular dilatation with poorer leaflet coaptation. This is accompanied by leaflet dysplasia at the zone of apposition, further affecting the coapting mechanism. This cycle of "regurgitation begets regurgitation" is broken by early intervention. As a counter argument to early repair, is the possibility of tearing of the sutures at the zone of apposition in those weighing less that 5kg at operation (Prifti et. al., 2004).

Until 1973, there had only been six attempts at repair of defects with a common orifice in those under the age of 6 years, and only two survivors. By the late 1990s, the timing had reached the contemporary practice of repair within the first six months of life.

With atrioventricular septal defect with separate orifices, in the absence symptoms and left atrioventricular valvar regurgitation, repair is performed effectively

at 3 to 4 years of age, in line with defects in the oval fossa. Surgery is suitably earlier in those presenting with symptoms before this.

Principles of repair

The goals of repair are ventricular septation, where there is a common orifice, atrial septation, together with repair of the atrioventricular valves, while avoiding heart block, residual defects and left ventricular outflow tract obstruction. The competence of the left atrioventricular valve must be achieved while preventing stenosis of its orifice.

Several techniques have been used to these ends, essentially being variations upon the single or double patch themes. However, unusual leaflet morphologies add to the complexity.

Approach to the heart, cannulation and cardioplegic arrest

The technique used at Great Ormond Street Hospital is described. After sternotomy and thymectomy, the pericardiotomy is veered slightly to the left of the midline.

The aorta, arterial duct and caval veins are then mobilized with the diathermy. A silk ligature is passed around the arterial duct once identified. In small infants, it may be a very delicate, so it is often not ligated until cardiopulmonary bypass is established. This is followed by insertion of 5/0 polypropylene purse string sutures in the aorta, superior caval vein and right atrial appendage.

For aortic cannulation, the flexible DLP cannula is used (Medtronic, Grand Rapids, Michigan). A temporary angled metal Great Ormond Street venous cannula (GU Company, Tricomed, Addiscombe, Surrey, UK) is placed through the right atrial appendage, allowing rapid establishment of cardiopulmonary bypass followed by

ligation of the arterial duct. The superior caval vein is cannulated with a second angled metal cannula appropriate for the calibre of the vessel. Following cannulation of the superior caval vein, the metal cannula is removed from the right atrial appendage and replaced with a vent. The inferior caval vein is then dissected to the first hepatic vein. Once exposed, a 5/0 polypropylene purse string is placed followed, by cannulation. Nylon tape then snares both caval veins.

The patient is cooled to 25° C in the case of the common orifice defect, and >32° C in the defect with separate orifices, and the aorta cross-clamped. Following cardioplegic arrest, the right atrium is opened with an incision running parallel to the right atrioventricular groove. Cold-blood cardioplegia is given every 20 minutes. The left atrium may be vented either through the oval fossa, or through the right superior pulmonary vein. This latter structure may be used eventually for the insertion of a left atrial pressure monitoring line.

The double patch technique

Irrespective of the patch technique, there are a number of initial stages prior to septation:

1. Inspection: this commences with the position and size of the coronary sinus, proceeding to the assessment of the size of the atrial component and patency of the oval fossa. The leaflets of the common atrioventricular valve are assessed for accessory orifices. The leaflets are elevated to reveal the ventricular component beneath as well as the state of the subvalvar apparatus. The ventricular septum is also inspected for additional septal defects.
2. Definition of the "kissing-points" (Figure 1.23): Bringing together the bridging leaflets over the left side of the ventricular septum allows their natural line of closure to be determined, forming a vital part of valvar repair. Once determined, these kissing points are marked with a 6/0 polypropylene suture.

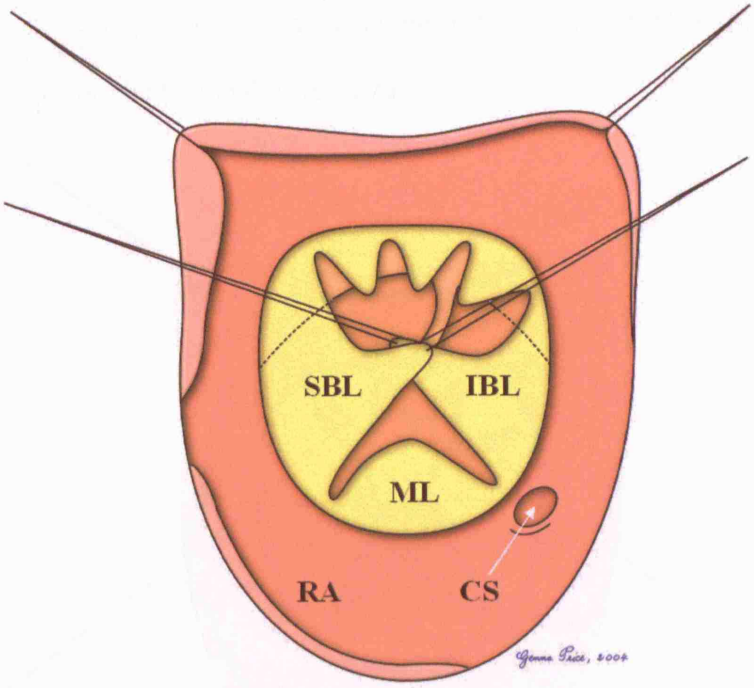

Figure 1.23 Illustration of the surgical repair of AVSD from the surgeon's perspective, through a right atriotomy (RA). The superior (SBL) and inferior (IBL) bridging leaflets are initially brought together at therir respective "kissing points" in order to fashion the new left atrioventricular valve

3. Closure of the ventricular component (Figure 1.24). This is closed with 0.4mm polytetrafluoroethylene (Gore-Tex), although other materials may be used. The dimensions of the defect are assessed using silk, which is used to fashion out a crescenteric patch of Gore-Tex. This is sutured to the right side of the ventricular septum with continuous 5/0 polypropylene. To facilitate this, some small secondary cords may have to be sacrificed. The suture line is commenced close to the annulus through the inferior bridging leaflet, where it is well away from the position of the bundle. The first one or two bites are placed with the patch outside the heart. One fixed, it is slid into position beneath the bridging leaflets. The suture line then runs deeply along the right side of the septum towards the superior bridging leaflet,

weaving through the cords. Finally, it is brought through the superior bridging leaflet, avoiding the aortic valve. A rubber-shod clamp is placed on the free end of the suture.

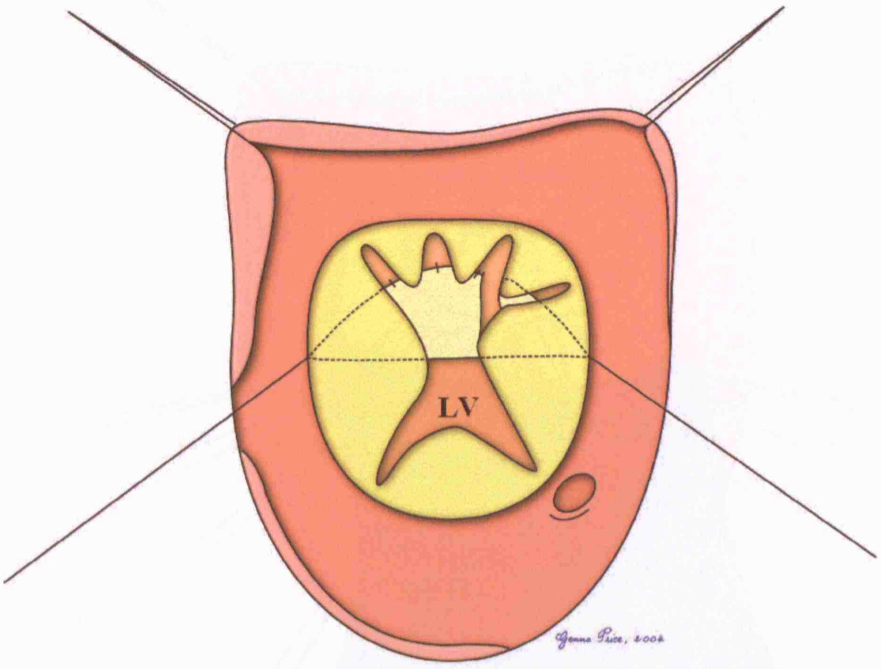

Figure 1.24 Ventricular septation using a cresenteric-shape piece of Gore-Tex. This is sutured to the right side of the ventricular septum. The remaining ends of the suture on either end is kept free in order to tie onto the atrial suture

4. Atrial septation (Figure 1.25). This is septated while separating the common valve into right and left components. Interrupted 6/0 polypropylene sutures, double armed, are placed along the horizontal margin of the ventricular patch. The sutures are then passes through the bridging leaflets, and then through the edge of the divided autologous pericardium. This suture line runs from the inferior to the superior margin of the annulus. Thus, the line passes in an axis that bisects the common

junction, its axis defined by the kissing points of the bridging leaflets. The sutures are then tied, after the right side of the pericardium is detached.

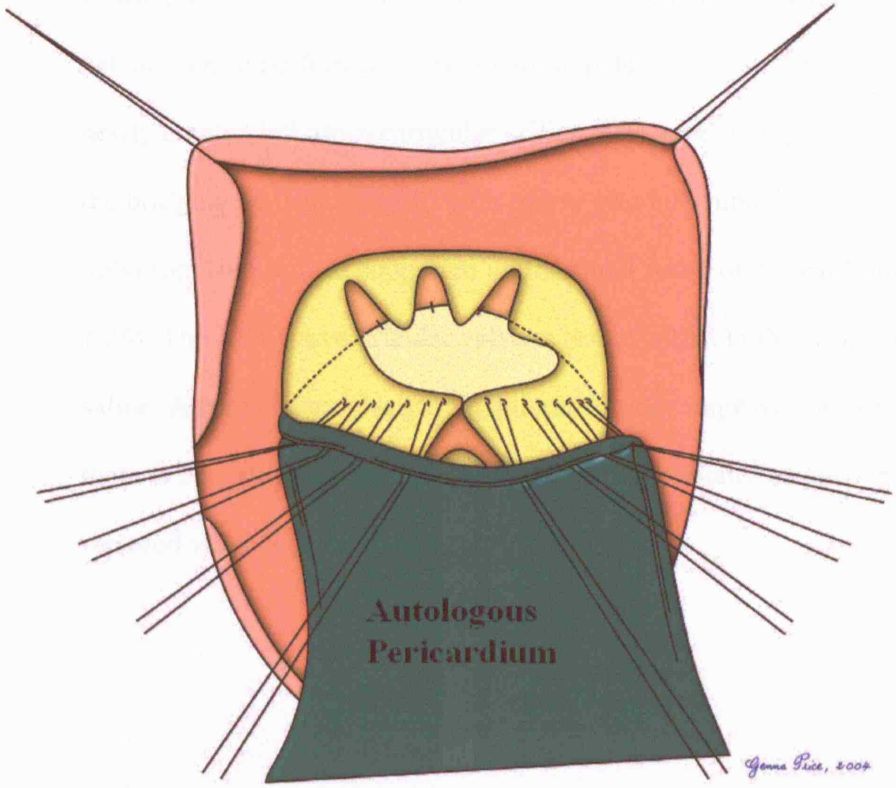

Figure 1.25 The pericardial patch in the atrial position is secured to the atrioventricular valves and ventricular septal patch with multiple interrupted double-armed sutures. The patch is then detatched from the rest of the pericardium

5. Consequently, the bridging leaflets are sandwiched between the two septal patches. Once performed, the pericardial patch is swung over, exposing the newly created left atrioventricular orifice. The zone of apposition between the bridging leaflets is closed with one or two interrupted 6/0 polypropylene sutures supported with a small patch of pericardium (Figure 1.26). The left atrioventricular valve is tested with a bulb syringe of cold saline. A commissuroplasty or annuloplasty may improve competence if there is persisting central regurgitation. A Hegar dilator ensures that the repaired valve is not stenotic.

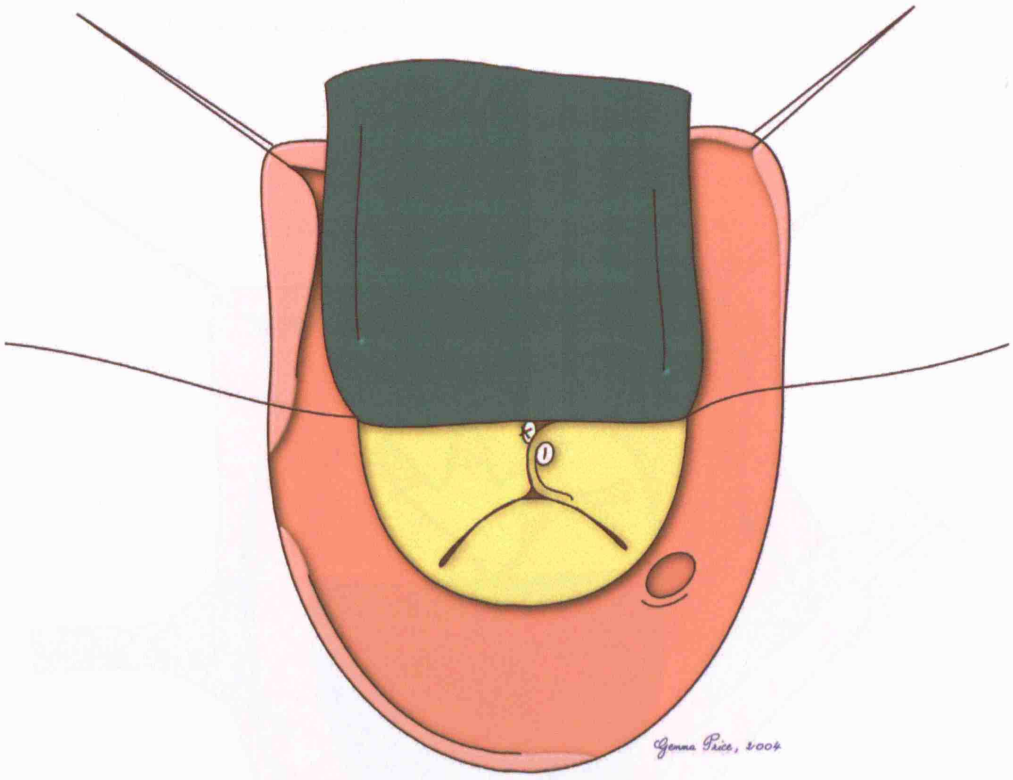

Figure 1.26 The anchored atrial septal patch is swung up to expose the leat atrioventricular valve. The zone of apposition is then closed with pledgeted interrupted sutures before testing the valvar competence

6. The atrial patch is sutured in place with continuous 5/0 polypropylene (Figure 1.27), avoiding the position of the atrioventricular node. The coronary sinus may be left on either side of the patch, but it is committed to the systemic venous chamber in the face of a left superior caval vein. The first suture of the atrial patch is the free end of the ventricular patch suture that was held in a rubber-shod clamp. If the coronary sinus is committed to the systemic venous chamber, the suture line passes around the coronary sinus, close to the Eustachian valve of the inferior caval vein, well inferior of the bundle. If the sinus is on the pulmonary venous

chamber, the suture line binds the patch to the left atrioventricular valve at the annular margin.

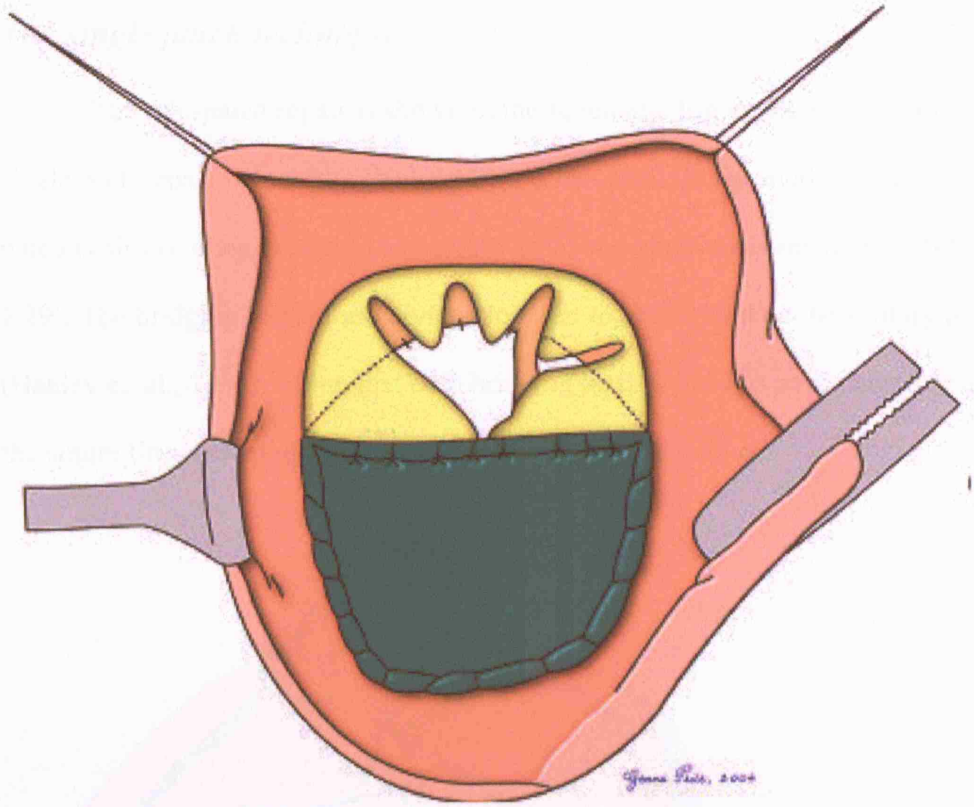

Figure 1.27 The left panel shows completion of intracardiac septation with suturing of the atrial patch to the rim of the primum defect, usually committing the coronary sinus to the left side.

Once the heart is septated, the aortic cross clamp is removed and de-airing commenced. Once warm, cardiopulmonary bypass is weaned

The single patch technique

The two-patch repair is shown in the schematic Figure 1.28. Compare with the single-path repair, which has changed little since 1962. In the modern era, a pericardial patch is almost always used to close both atrial and ventricular septal defects (Figure 1.29). The bridging leaflets are divided in order to accommodate the solitary patch (Hanley et. al., 1993). Given that both bridging leaflets have to be anchored to the patch, the suture line is more extensive than the two-patch technique.

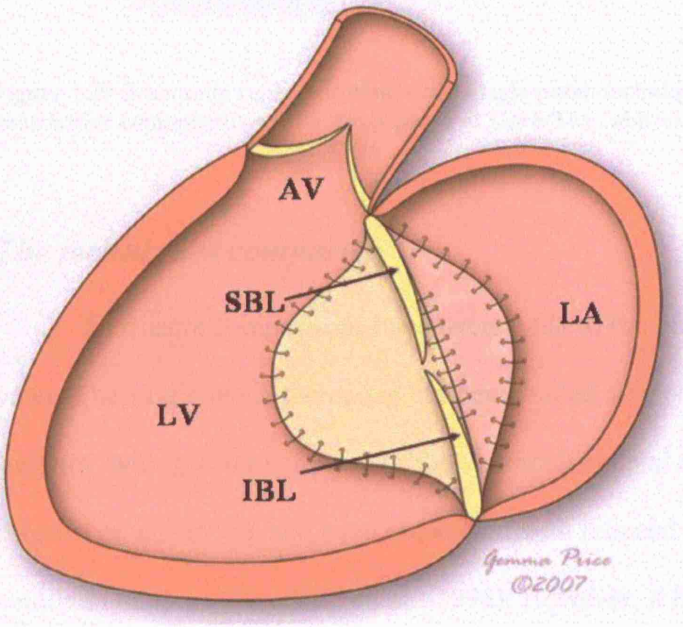

Figure 1.28 Schematic representation of the double patch technique as described above. AV, aortic valve; LV, left ventricle; LA, left atrium; SBL, superior bridging leaflet; IBL, inferior bridging leaflet

Figure 1.29 Schematic representation of the single-patch technique of repairing the atrial and ventricular components with a single patch of Gore-Tex . abbreviations as for Figure 1.28

The techniques compared

Extensive comparisons have been made of the benefits of one technique over the other. The single patch technique has been hailed as more simple, and therefore superior, with greater exposure of the ventricular septal defect and sub-valvar apparatus (Merrill et. al., 1991), and even associated with reduced duration of post-operative ventilator support (Tweddell et. al., 1996). However, it has also been criticised for its theoretical effects on valvar competence (Pacifico et. al., 1988) since relatively more of the left atrioventricular valve is taken up in the suture line with the risk dehiscence (Bando et. al., 1995; Culpepper et. al., 1978; Yasui et. al., 1990). This has caused some to change their technique over time (Bando et. al., 1995). Furthermore, it has been argued that closure of the zone of apposition may be inappropriate with this technique,

since division of the leaflets and re-suspension of the valve results in restricted mobility of the superior bridging leaflet (Ashraf et. al., 1993). Nevertheless, results are comparable and depend on operator preference (Reddy et. al., 1998).

The modified single patch technique

This was initially introduced by Rastelli, but refined and expanded by Wilcox (Wilcox et. al., 1997) and the Australian group (Nicholson et. al., 1999) (Figure 1.30). Here, the atrioventricular valves are sutured directly to the crest of the ventricular septum, simultaneously incorporating a single patch that is anchored to the leaflets, closing the atrial septal defect. Thus, in essence, the defect with the common orifice is converted to one with separate orifices where the valves are bound to the septal crest.

Several centres have adopted it as their standard, including Boston (Jonas, 2004) who have based their arguments on anatomic principles. Although it is known that the septal scoop is greatest in the setting of a common orifice, in 30-40% of hearts this is not the case (Ebels et. al., 1990). It follows, therefore, that direct suturing of the leaflets to the septal crest is entirely feasible without distortion of the left ventricular outflow or disruption of the natural line of valvar closure. Another argument for this simplified technique is that ventricular septal patches having been getting progressively smaller with time, so discarding them is a natural step in surgical evolution.

Figure 1.30 Schematic representation of the modified single patch technique. Here, the bridging leaflets are brought down to the crest of the ventricular septum, thus closing the ventricular component. The atrial component is closed with autologous pericardium. Abbreviations as for Figure 1.28

Attaining and maintaining left atrioventricular valvar competence

Attaining a competent left atrioventricular valve involves more than closure of the Zone of Apposition between the bridging leaflets.

Correct ventricular patch sizing is the first method, since it supports the annulus. If the patch is too long, the bridging leaflets will fail to coapt. If too short, valvar stenosis will ensue (Lacour-Gayet et. al., 1991).

Despite the observation that the Zone of Apposition is the most incompetent part of the left atrioventricular valve, its closure has not always been advocated. Carpentier (Carpentier, 1977) has stated that the trifoliate left atrioventricular valve is well adapted to its role. Thus, closure of its Zone of Apposition valve would reduce its opening during diastole, and produce undue tension in the suture line. (Ashraf et. al., 1993;

Enriquez de Salamanca et. al., 1977). Therefore, an integrated tri-leaflet repair was advocated, based on the native trifoliate appearance.

Nevertheless, others have argued that the zone does not have the characteristic features and support of commissures in the normal atrioventricular valves, and so should be closed (Capouya et. al., 1992).

Others have taken the middle ground, repairing only those valves that were incompetent on saline testing. (Bove et. al., 1984; Mavroudis et. al., 1982), and not repairing those valves in small infants because of the risk of tearing the leaflets (Prifti et. al., 2004).

There are certain situations where it is agreed that the zone should be left open to prevent valvar stenosis. One well recognized situation is that of the solitary left ventricular papillary muscle, or so-called parachute valve. Here, the bridging leaflets have a common papillary muscle insertion, leading to a slit-like valvar orifice. There is a similar risk of stenosis when faced with a small left ventricle or in the presence of an accessory left ventricular orifice (Abbruzzese et. al., 1990; Ebels et. al., 1990; Mace et. al., 2001; Meijboom et. al., 1986). One way of standardizing the decision as to close has been to assess the size of the left mural leaflet, the angular size of which has been found to be inversely related to the size of the inferior bridging leaflet (Ebels et. al., 1990). An angular size of greater than 45° has been used as the determinant of zone closure (Ebels et. al., 2002).

Commissuroplasty or annuloplasty may also be used to improve competence, either at the commissures, or centrally. They have also been used as a "belt and braces" measure in older patients with the defect with separate orifices where there has been chronic annular dilatation (Capouya et. al., 1992; Reddy et. al., 1998).

Atrioventricular septal defect with tetralogy of Fallot

Tetralogy of Fallot complicates 2.7-10% of cases of atrioventricular septal defect. Conversely, atrioventricular septal defect complicates only 1-2% of cases of tetralogy of Fallot (Karl, 1997). There are a number of issues that need to be considered during repair.

Firstly, is the issue of whether complete primary can be carried out at an early stage. Even in the contemporary era, the majority of patients are palliated initially with a systemic to pulmonary shunt, the decision being guided by the severity of pre-operative cyanosis. However, some have advocated early primary repair where possible stating that this aggressive strategy negates the risks associated with shunting (McElhinney et. al., 1998). However, there is no consensus, so that the age at complete repair varies greatly among different centres, ranging from a few months to several years.

Another issue, is the finding that in the combined defect, superior bridging leaflet is free-floating (Suzuki et. al., 1998). This has impacted the decision as to whether to use a single or double-patch strategy (Ilbawi et. al., 1990; McElhinney et. al., 1998). Some advocate two-patch repair on the understanding that it reduces the incidence of left ventricular outflow tract obstruction (Alonso et. al., 1990; Bertolini et. al., 1996; Chiu et. al., 1995; Vouhe et. al., 1986). This is because the ventricular septal patch can be fashioned into a tear-drop shape easily to accommodate the contour of the deviated outlet septum. Given this and other unresolved issues, such as the impact of both atrioventricular and pulmonary valvar dysfunction, mortality is still highly variable, ranging from less than 5% (Alonso et. al., 1990; Karl, 1997) to 33% (Bertolini et. al., 1996).

Post-operative complications

Aside from the general risks associated with anaesthesia and cardiopulmonary bypass, common with this defect:

- ***Pulmonary hypertensive crisis***: the incidence of this complication has fallen with the advent of reduced age at primary repair, but the risk is still significant in older patients, those with pre-operative pulmonary hypertension and those with moderate to severe pre-operative left atrioventricular valvar regurgitation. In these cases, concurrent use of both pulmonary artery and left atrial pressure lines are invaluable in the first 24-36 hours after surgery. Scenarios that may trigger a crisis, such as acidosis, hypoxia or agitation must be avoided. Thus, older patients are intubated and sedated for longer. Alpha-adrenergic blockers, such as phenoxybenzamine, or phosphodiesterase inhibitors such as milrinone may be used.

  During a crisis, the patient is sedated, and hyperventilated so that the pCO_2 falls to below 3.5kPa. Paralysis may also be instituted together with intravenous nitroprusside or inhaled nitric oxide.

- ***Heart block*:** In the modern era, when the position of the conduction bundle has now been defined, the prevalence of this complication has fallen to 1-2%. The key is careful suture placement in the region of the coronary sinus, remembering that the conduction system runs the same course irrespective of the number of orifices.

  Following operation, the patient should leave the operating room with temporary pacing wires, in the case of temporary heart block that may occur in the context of regional conduction tissue oedema.

- ***Left atrioventricular valvar regurgitation***: this may be considered as an early or late postoperative complication, that requires re-operation. It may be recognised as a persistently elevated left atrial pressure and failure to wean from intubation, being confirmed by echocardiography.

  Early re-operation for regurgitation has been consistently been reported in 5-7% of patients, with little change over the years (Hanley et. al., 1993; Michielon et. al., 1995; Redmond et. al., 1996). It may be associated with technical factors, such as not closing the zone of apposition, but in some series, the use of closure of the zone with annuloplasty did not affect the overall incidence of regurgitation (Hanley et. al., 1993). Some have also suggested that the severity of pre-operative regurgitation correlated with the severity post-operatively (Bando et. al., 1995), whereas others have found no relationship between the two (Weintraub et. al., 1990).

  Late regurgitation, measured as freedom from re-operation, is found with varying degree, ranging from about 80-90% at 10 years (Boening et. al., 2002; Crawford, Jr. et. al., 2001; Gunther et. al., 1998). The incidence of this complication has similarly shown little change over the years, being more common in various situations, such as in the setting of a double orifice valve, non-closure of the zone of apposition, and non-Down's patients (Michielon et. al., 1995; Ross et. al., 1991) and a dysplastic left atrioventricular valve. Recently, division of the superior bridging leaflet at operation during patch placement has also been associated with an increased incidence of long term left atrioventricular valve regurgitation (Fortuna et. al., 2004). Table 6.5 summarizes the risk factors identified for early and late atrioventricular valvar regurgitation by different investigators.

The Future

Although, in terms of mortality, the surgical repair of this defect has come a very long way, the main issue in the future involves long-term durability of the repair and quality of life. With this in mind, the persisting incidence of long-term left atrioventricular valvar deterioration will only be tackled successfully by thoroughly understanding the form and function of the valve with all of its morphologic nuances.

Chapter 2: Review of the specimens with atrioventricular septal defect with common junction at the Cardiac Archive of Great Ormond Street Hospital

Introduction

Within the Cardiac Archive of the Institute of Child Health there are over 2000 cardiac specimens dating back to the early 1960s. Those with atrioventricular septal defect with common atrioventricular junction were anlaysed.

Methods

Inclusion and exclusion criteria were formulated initially and the analyses performed using 2.5X optical magnification loupes on a wide-angle lens (Designs for Vision Inc., Ronkonkoma. NY, USA).

In all cases, previous dissection obviated the need for further exposure. The left ventricle was usually exposed through a curvi-linear incision from the left atrioventricular junction to the apex, bisecting its parietal wall and left mural leaflet. This axis also separated the papillary muscles. In the remainder of the specimens, the incision passed around the ventricular wall from anterior to posterior, in the axis of the ventricular septum, thus creating a flap of parietal wall containing both papillary muscles and the left mural leaflet. The former mode of exposure was better for demonstrating the coapting surfaces of the bridging leaflets, and the latter, for exposing the subvalvar apparatus.

Photography

Where appropriate, digital images were acquired using a Nikon Coolpix 5700 digital camera (Nikon Corporation, Tokyo, Japan). The stored images were then converted to the Tiff format, and labelled using Microsoft PowerPoint.

Inclusion Criteria

There were several criteria identified

- Specimens exhibiting an atrioventricular septal defect with common atrioventricular junction, either with separate or solitary atrioventricular orifices
- Specimens of any age and size
- Irrespective of previous surgical intervention (ranging from pulmonary trunk banding to complete intracardiac repair)
- Specimens with or without pulmonary attachment
- Those coming from patients of any karyotype

Exclusion Criteria

- Specimens that were in multiple pieces in the bucket
- Presence of a prosthetic left atrioventricular valve
- Specimens exhibiting isomerism of the atrial appendages. This was due to the often small and heavily-dissected nature of the specimen precluding sound and consistent examination.
- Those with torn or avulsed leaflets of the left atrioventricular valve

Once identified, specimens were catagorised and analysed with respect to:

1. The presence of a common or separate atrioventricular orifices
2. Any previous surgical intervention, including pulmonary trunk banding
3. The mode of complete repair, where relevant
4. Ventricular morphology:

- *Ventricular balance* – whether the ventricles were of the same size, as judged externally

Features of the bridging leaflets:

- *Degree of bridging of the superior bridging leaflet into the right ventricle, expressed as the Rastelli Class (Rastelli et. al., 1966)*
- *Degree of bridging of the inferior bridging leaflet, and whether it was divided over the crest of the ventricular septum*
- *The morphologic features of the coapting surfaces of the bridging leaflets at the zone of Apposition*
- *The cordal support to the Zone of Apposition*

5. The presence and location of any accessory left ventricular valvar orifices
6. The presence of a solitary left ventricular papillary muscle arrangement
7. Morphology of the atrial and ventricular septums:
    - *Presence of a defect within the oval fossa*
    - *Any deviation of the outlet septum, and patency of the right ventricular outflow tract*
    - *Presence of a muscular ventricular septal defect*
8. Associated abnormalities, such as
    - Left superior caval vein
    - Abnormalities of the great vessels

Results

There were a total of 121 hearts with atrioventricular septal defect with common atrioventricular junction. Twenty-three of these were excluded from further analysis on the criteria demonstrated on Table 2.1. The principle reason was heavy dissection precluding any meaningful examination. Thus, 98 hearts underwent detailed morphologic review.

Reason for Exclusion	Number
Heart in Multiple Pieces	9
Intracardiac Dissection or Damage	4
Isomerism of the Atrial Appendages	6
Small and dry specimen	1
Double inlet left ventricle	2
Prosthetic Left Atrioventricular Valve	1

Table 2.1. Reasons for excluding 23 specimens from the collection from morphologic analysis

Separate and common valvar orifices

Among the 98 specimens examined, 72 hearts exhibited a common atrioventricular valvar orifice, and 26 separate orifices. Those defects that had previously been described as the so-called intermediate defect were categorized here under defects with a common orifice.

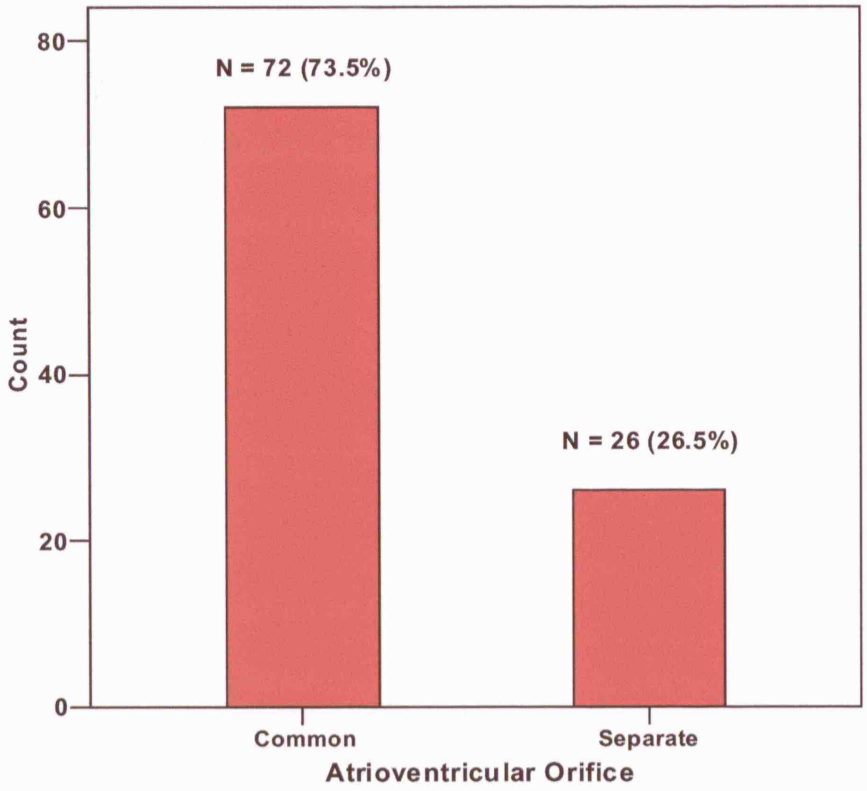

Figure 2.1 Histogram demonstrating the number of each type of atrioventricular septal defect with common atrioventricular junction

Arrangement of the bridging leaflets

For defects with a common atrioventricular orifce, the most frequent arrangement of the superior bridging leaflet was the Rastelli Type A variety, being observed in 32 hearts (44.4% of those with a common orifice). The Type B arrangement, the least common variety was observed in only 8 hearts (8.3%). The Type C arrangement was seen in 14 hearts (19.4%). In 18 hearts (25% of those with a common orifice) the degree of bridging could not be determined due to previous repair.

In both defects with common and separate orifices, the most common arrangement of the inferior bridging leaflet was where the leaflet straddled the

ventricular septal crest evenly without being divided over it. This was seen in 18 hearts with a common orifice and 11 (42.2%) hearts with separate orifices (Lee et. al., 1985). A completely free-floating inferior bridging leaflet was never seen and the degree of tethering ranged from cordal attachment to direct leaflet adhesion to the septum.

Surgical intervention

Table 2.2 summarizes the prevalence of previous surgical intervention on the specimens.

Orifice	Previous Surgery	Frequency	Percent
Common	Yes	39	54.2
	No	33	45.8
	Total	72	100.0
Separate	Yes	14	53.8
	No	12	46.1
	Total	26	100.0

Table 2.2 shows the prevalence of previous surgical intervention

In the cases with a common atrioventricular orifice, 6 of the cases (8.3% of total common orifice cases) demonstrated previous pulmonary trunk banding. In one case, the great vessels were divided close to the arterial valves, making evidence of previous palliation uncertain. In two of these cases, the band co-exited with previous aortic arch repair in the context of a small left ventricle and solitary papillary muscle arrangement.

For hearts with separate orifices, 3 demonstrated previous pulmonary trunk banding, one in association with previous aortic arch repair in the context of a small left ventricle and solitary papillary muscle arrangement.

Aside from previous intracardiac patch repair, other additional, non-palliative surgery included, total cavo-pulmonary connection in two cases (one with separate orifices and a small left ventricle, one with a common orifice and a small right ventricle); prosthetic replacement of the right atrioventricular valve in one case, and muscular resection of the left ventricular outflow tract for sub-aortic stenosis in one case.

Associated cardiac malformations

A number of additional cardiac malformations were identified:

Associated Cardiac Defect	In Hearts with a common orifice	In Hearts with Separate Orifices
Defect in the Oval Fossa	**29/72 (40.3%)**	**5/26 (19.2%)**
LVOTO	**17/72 (23.6%)**	**5/26 (19.2%)**
Tetralogy of Fallot with Pulmonary stenosis	**2/72 (2.7%)**	***N/A***
mVSD	**2**	***0***
DORV	**9/72 (12.5%)**	***N/A***
LSCV	**0**	**1/26 (3.8%)**
TAPVC	**0**	**1/26 (3.8%)**

Table 2.3 Associated Cardiac Malformations. LVOTO, left ventricular outflow tract obstruction; DORV, double-outlet right ventricle; mVSD, mid-muscular ventricular septal defect; TGA, transposition of the great arteries; LSCV, left superior caval vein; TAPVC, totally anomalous pulmonary venous connection

In some instances, these figures are probably not a true reflection of the actual number of associated abnormalities. For example, in 19 out of the 98 cases (19.4%) it was not possible to determine if there was a defect in the oval fossa owing to the manner of atrial dissection. However, this was still the most common associated anomaly, being observed in 29 (40.3%) hearts with a common orifice, and 5 (19.2%) hearts with separate orifices. In those instances where it was very large, the primum septum beneath looked no more than a muscular bar over the bridging leaflets. The next most common defect were those occurring due to deviation of the outlet septum, the tetralogy of Fallot

in 2 cases, and double-outlet right ventricle in 9 cases. In all of these cases, the superior bridging leaflet was of the so-called Rastelli type C variety. In two specimens, the right ventricular outflow tract was repaired with an outflow tract patch. Five specimens exhibited deviation of the outlet septum without pulmonary stenosis or double outlet.

Left Ventricular Outflow Tract Obstruction (LVOTO)

For the purposes of this study, this was divided into subaortic stenosis, stenosis at the valvar level, coarctation, hypoplastic aortic arch and interrupted aortic arch. Such anomalies co-existed with a small left ventricle and solitary arrangement of the papillary muscles.

Aetiology of LVOTO	Number of cases	Associated with small Left Ventricle	Associated with Solitary papillary Muscle
Subaortic Stenosis	5	1	0
Coarctation	8	7	3
Hypoplastic Arch	8	4	5
Interrupted Arch	1	0	0

Table 2.4 this shows the different aetiologies of left ventricular outflow tract obstruction encountered, and how many of those were associated with a small lewft ventricle and solitary papillary muscle arrangement of the left ventricle

In 21 out of the 98 cases (21.4%) it was not possible to determine aortic morphology owing to dissection of the great vessels, so that the final results shown may not reflect the true incidence in this series. All 5 cases of subaortic stenosis were due to anomalous extension of the superior papillary muscle into the left ventricular outflow tract. In one of these cases, there was evidence of previous muscular resection of the outflow tract. Only one occurred in association with a small left ventricle. Coarctation, with or without previous repair of the aorta was seen in 8 cases, 7 of these were associated with a small left ventricle, and in 3 with a solitary papillary muscle arrangement. Interruption of the aortic arch was seen in only 1 case, where the ventricles were balanced, but with deviation of the outlet septum without right ventricular outflow tract obstruction.

Unusual morphologic variants: ventricular imbalance, dual orifice and the solitary papillary muscle arrangement

Ventricular imbalance

Sixty-two percent of the defects with a common atrioventricular orifice exhibited balanced ventricles, a comparable proportion to the defect with separate orifices. Similarly the distribution of small right and small left ventricles were similar among the different types of defect. Thus, left ventricular hypoplasia was found in 26.4% of defects with a common orifice, compared to 30.8% of defects with separate orifices. Likewise, a small right ventricle was observed in 11.1% of defects with a common orifice, and 7.7% of defects with separate orifices. (Table 2.5)

Type of Orifice	Ventricular size relationship	Frequency	Percent
Common	*Balanced*	45	62.5
	Small LV	19	26.4
	Small RV	8	11.1
	Total	72	100.0
Separate	*Balanced*	16	61.5
	Small LV	8	30.8
	Small RV	2	7.7
	Total	26	100.0

Table 2.5 Shows the ventricular size relationships in defects with common and separate orifices

Left ventricular hypoplasia was also often observed in association with the constellation of defects causing left ventricular outflow tract obstruction, solitary papillary muscle of the left ventricle and accessory left ventricular orifices. The solitary left ventricular papillary muscle arrangement was found in 15 (20.8%) specimens with a common atrioventricular orifice compare to 8 (30.8%) cases with separate orifices. In two of these cases, there had been univentricular repair with total cavopulmonary connection. In four cases, there was frank stenosis of the left atrioventricular valvar orifice, in three of these cases due to surgical repair of the left atrioventricular valve.

Accessory orifices

An accessory orifice of the left atrioventricular valve was observed in 5 cases with a common atrioventricular orifice (6.9%) and 2 cases with separate orifices (7.7% of cases with separate orifices). In all of these cases, this orifice was formed by union of the inferior bridging and mural leaflets, being located over the inferior papillary muscle. One case of accessory orifice was found in combination with a small left ventricle, solitary papillary muscle arrangement and left ventricular outflow tract obstruction. (See Figure 2.2)

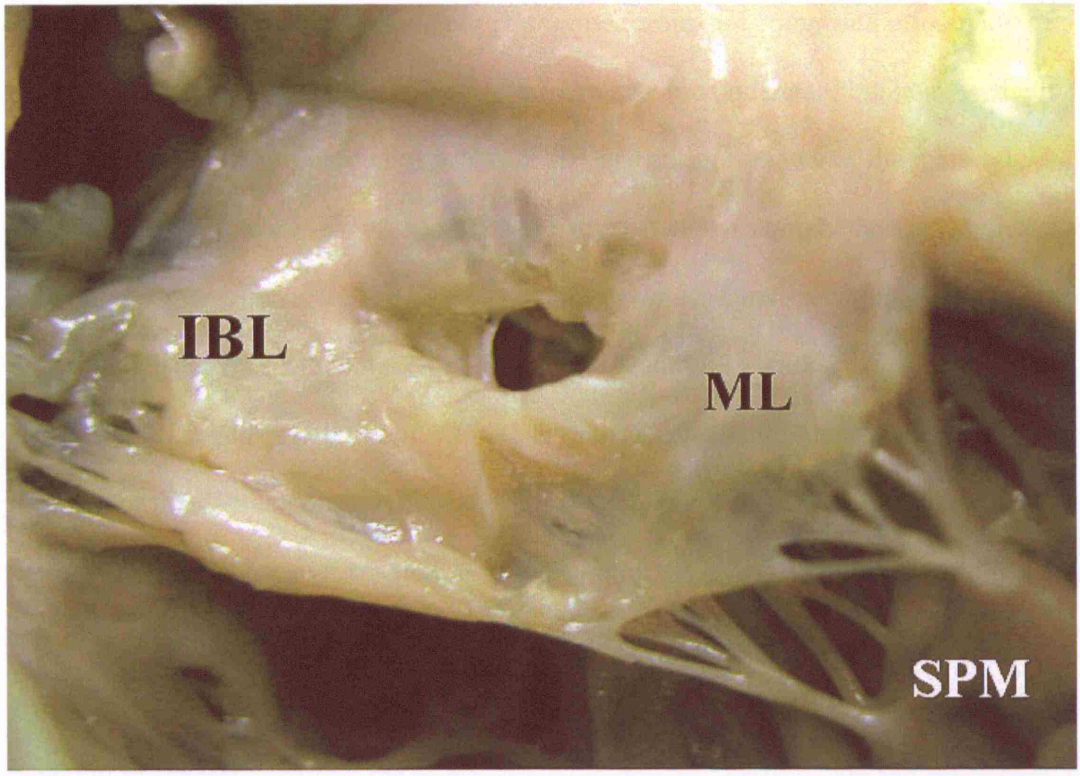

Figure 2.2 Accessory orifice of the left atrioventricular valve looking from the left ventricular aspect of the ventricular septum. In this instance, the orifice was formed by the fusion of the inferior bridging leaflet with the mural leaflet

Conclusions and use of specimens for further, detailed analysis

Aside from this collection, the other major collections of congenitally malformed hearts are housed at the Royal Brompton Hospital, London; the University of Amsterdam, the Netherlands; The Children's Hospital, Pittsburgh, PA, USA; Boston Children's Hospital, Boston, MA, USA; and the Mayo Clinic, Rochester, MN, USA. Previous studies of atrioventricular septal defect with common atrioventricular junction from these collections have provided a broad understanding of many different aspects of this defect. These studies can be essentially divided into descriptive studies, and those that employ morphometric techniques. The former group are composed principally of the earliest observations of the defect. As experience and understanding increased with time, the latter studies emerged. It is hoped that this current review of the material available will form the basis of the next generation of study- namely detailed analysis of how the form may influence the function, and how detailed understanding will individualize the surgical approach to the left atrioventricular valve.

The size and variability of the collection was considered more than adequate to provide for the detailed observations that form the basis of this thesis. Furthermore, there were very few specimens that were rejected on the basis of quality. Thus, in the majority of cases, subvalvar apparatus was preserved enough to provide for some crucial observations. Where further material was required, such as in the case of the defect with separate orifices, the numbers analysed were fortified with the specimens of the collections from the USA.

What is more difficult to fathom objectively is how the specimens of any collection represent the true morphologic picture. Undoubtedly, these specimens are a self-selecting population consisting of the most severely abnormal examples of the

defect. For this reason, where possible, some of the observations made were supplemeted by images taken from the operating room of the living morphology.

Chapter 3: The Mitral Valve

Section 3.1: The morphology of the mitral valve: retrospective analysis of yesterday's future

Introduction

Morphological understanding has always provided the basis for optimal surgical practice, and this is nowhere truer than with the mitral valve. The current trend towards preservation and repair of the native valve, where possible, has laid bare conspicuously inconsistent practice and unresolved issues when describing the mitral apparatus, particularly by echocardiographers when determining the options of repair as opposed to replacement (Alexi-Meskishvili et. al., 1997). Problems are magnified by the different viewpoints employed when morphologists, surgeons, and echocardiographers describe the mitral valve.

Structure of the valve

The mitral valvar apparatus both, functionally and morphologically, consists of a constellation of individual structures, each of which is vital to its overall function. This complex consists of the annulus, the leaflets, the tendinous cords and the papillary muscles. To this may be added the left atrial wall, whose integrity influences the function of the annulus and the supported leaflets (Perloff et. al., 1972).

Although more D-shaped than circular, the mitral annulus functions as a complete ring to which the leaflets are anchored. The flattened portion of the ring is made up of regions of the leaflets of the aortic and mitral valve. The right trigone is somewhat larger and firmer than the left, with the propensity towards age related

calcification. In fact, this structure is ossified in bovines, forming the "os cordis." (James, 1965) Moreover, the point of unity of the right fibrous trigone with the membranous septum marks the so-called central fibrous body of the heart, which is pierced by the atrioventricular conduction axis. The remainder of the annulus continues around the parietal part of the left atrioventricular junction to form a flexible ring. In places, the annulus takes the form of a collagenous rod that supports the mural leaflet of the valve, but in other areas, the annulus is more of a fold, or else deficient (Perloff et. al., 1972). Externally, the position of the annulus is delineated by the courses of the coronary sinus and the circumflex branch of the left coronary artery running in the atrioventricular groove (Figure 3.1). These are important points to remember during valve replacement and manual decalcification of the annulus when these structures can become injured. The relationship to the coronary artery is more intimate when the circumflex artery is dominant.

The flexible, but supportive, nature of this ring defines the basis for its principle functions – to provide a firm origin to the leaflets, and to act as a dynamic component to the competence mechanism that comes into play during ventricular systole. Passive contraction of the ring at this point of the cardiac cycle ensures that the leaflets it supports coapt more firmly (Perloff et. al., 1972). An understanding of the pathophysiology of annular dilation, and its contribution to valvar incompetence, has revealed that the strength is not uniformly distributed throughout the ring. Angelini showed that the fibrous support of the annulus arises ostensibly from the fibrous trigones, and embraces the ring to a variable degree (Angelini et. al., 1988). That this fibrous embrace may be incomplete may explain why the posterior portion of the ring is most greatly affected by progressive dilation, in contrast to the area of the aorto-mitral

fibrous continuity, whose length is remarkably consistent even in severe annular dilatation (Kumar et. al., 1995).

Before any anatomic structure can be described without ambiguity, it must first be oriented in space with reference to a standardized and uniformly understood framework. In the case of gross anatomy, the accepted plane is the so-called anatomic position. All structures can then be described on the basis of three orthogonal planes, which run from anterior to posterior, from superior to inferior, and from medial to lateral. Organs such as the heart, however, whose axes have rotated away from the long axis of the anatomic position, have traditionally been described in terms of their own orthogonal planes. In clinical practice this can be confusing and interfere with understanding. A good case in point regards the positions of the papillary muscles of the mitral valve. Traditionally referred to as the anterior and posterior muscles, or else, anterior-medial or postero-lateral, simple comparison with the arrangement as seen in left anterior oblique orientation establishes immediately deficiency of this approach. When compared to the structures of the body, the so-called anterior muscle is in fact more posterior than its counterpart! As can be seen from Figure 3.1, these muscles are really positioned supero-posteriorly and infero anteriorly. Adoption of this attitudinally correct designation will leave little room for diverging interpretations among morphologists, surgeons, and echocardiographers.

Figure 3.1: The so-called anterior papillary muscle, in reality, is positioned supero-posteriorly relative to its counterpart when considered in the orthogonal planes of the body. Courtesy of Robert H. Anderson

The leaflets also assume a more oblique position than their traditional names "anterior" and "posterior" suggest. The form and function of the antero-medial, better termed the aortic, leaflet has been well documented. Its upper margin is in fibrous continuity with two of the leaflets of the aortic valve. Its rounded lower end hangs free to separate the inflow and outflow components of the left ventricle. On either side of the free edge, tendinous cords tether it on either side to the respective papillary muscles. When viewed from the atrial side, the aortic leaflet is seen to guard one-third of the circumference of the annulus, but since it is also much deeper than its counterpart, the overall orificial area covered by each leaflet is equal (Ranganathan et. al., 1970).

The postero-lateral, better termed the mural leaflet, has a more variable appearance. This fact, together with its importance with respect to surgical repair, has

ensured that it lies at the epicentre of the controversy surrounding the mitral valve. When viewed from the atrial side, the mural leaflet has at least three slits on its free edge. When viewed in the open position, as has been the pathological and anatomical tradition (Figure 3.2), these indentations constitute scallops, whose free margins run to within a half of a millimetre of the annulus (Ho, 2002).

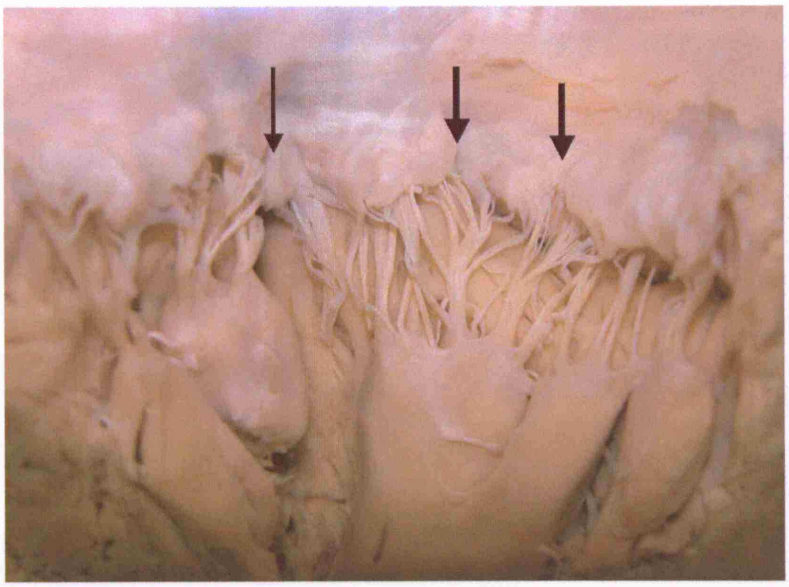

Figure 3.2 The morphologist's view of the opened mitral valve, showing the indentations (arrows) in the mural leaflet that extend towards the annulus, albeit not reaching the atrioventricular junction. This produces a scalloped appearance for the mural leaflet

At issue is whether these scallops should be considered as individual leaflets in their own right (Yacoub, 1976), or whether they are mere sub-divisions of one long, solitary mural leaflet (Carpentier, 1983; Victor et. al., 1994). The variability in the size and number of these scallops or slits is best appreciated when closed valve is viewed from the atrial aspect, as seen by the surgeon (Figure 3.3). This shows that a solitary cavo-convex zone of apposition exists between the mural and aortic leaflets. When

considered in the literal sense - that of junctional zones - this line represents the true commissure of the valve. This zone of apposition is directly comparable to the single commissure seen between the lips of the mouth, or between the eyelids (Anderson et. al., 1995). This is quite distinct from the current trend of denoting the ends of the locus between the two leaflets as commissures, giving the mitral valve two commissures (Ranganathan et. al., 1970).

Figure 3.3 The anatomic arrangement of the mitral valve as seen by the surgeon. The aortic and mural leaflets coapt along a solitary primary zone of apposition. There are slits in the mural leaflet that permit snug closure of the valve. Some have suggested that this is best interpreted on the basis of the valve having more than two leaflets (see Figure 3.4). Irrespective of this, the valve has only one line of primary closure. Note that the two ends of this primary line of closure do not extend to the annulus. Courtesy of Robert H. Anderson

Taking these points into account, a fundamental question that has divided expert opinion is the nature of the slits in the mural leaflet. If the mural leaflet is considered as a solitary structure, as has been the anatomic custom, then the slits are the zones of apposition between different areas of the same valve, analogous to creases formed when

a handkerchief is placed in a napkin-ring, or the pleats of a skirt (Victor et. al., 1994).Ultimately, they would function in unison, as secondary zones of apposition between adjacent parts of the mural leaflet that permit more competent closure between the mural and aortic leaflets. Recent experience with surgical repair of the mitral valve has brought this question to the forefront.

In the current era, the surgeon has become the anatomist, viewing anatomic structures in their natural state, placing them in their functional contexts with greater certainty. The questions posed, and the solutions offered, concerning the number and nature of the leaflets have direct relevance to surgical practice. They are also deserving of consideration by the echocardiographer. During repair of the mitral valve, each of the scallops has to be managed a separate entity. It is known that the central scallop of the mural leaflet has a greater propensity to prolapse than the others (Carpentier, 1983).With this understanding in mind, together with the multi-leafleted appearance of the valve during operative inspection, many surgeons have suggested that the mitral is not, in fact, a bifoliate valve, as once envisaged. As already discussed, Yacoub (1976) described a mitral annulus as guarded by four leaflets, each scallop, as seen by the anatomist, as being a separate entity (Figure 3.4A). The group of Duran (Kumar et. al., 1995) extended this classification to include the two additional leaflets seen at the two ends of the solitary junction between the mural and aortic leaflets, making a mitral valve with six leaflets Figure 3.4B). The classification used most commonly, nonetheless, continues to recognize two leaflets, but divides the leaflets in alphanumeric fashion (Figure 3.4C), acknowledging the tripartite division of the mural leaflet (Carpentier, 1983). The one finding that diminishes this multi-leaflet concept, irrespective of its popularity is that, in some instances, when viewed from above, as seen by the surgeon, the mitral possesses multiple slits, rather than three, along its mural aspect. Does each of

these represent yet more leaflets? And what of the situation of isolated cleft of the aortic leaflet of the mitral valve, which produces a bifid appearance to the leaflet in the setting of normal atrioventricular septation? (Anderson et. al., 1985). When faced with a complex problem with multiple and competing answers, it is usually the simplest explanation that remains the most faithful to the truth – hence our own preference to consider the valve as possessing two leaflets closing along a solitary zone of apposition (Figure 3.3).

Figure 3.4 The valve shown in Figure 3.3 has been copied to illustrate the concepts for description suggested by Yacoub et. al. (Panel A), arguing that the valve has four leaflets, and Duran and colleagues (Panel B), who suggested that there are six leaflets when consideration is taken of the "commissural areas". More commonly, however, surgeons adopt the suggestion of Carpentier (Panel C) who labelled the functional components of the valve in alphanumeric fashion. Irrespective of the concept adopted, it remains the case that the valve possesses one zone of primary closure between its component parts. Courtesy of Robert H. Anderson

Since the earliest days, beginning with Da Vinci, investigators have understood that the competence afforded by the leaflets of the mitral leaflets is only as good as the

tendinous cords that support them. Over the last several decades, investigators have detailed the morphology of these structures (Lam et. al., 1970a). In more recent times, others have demonstrated their function in the living heart (Obadia et. al., 1997; Timek et. al., 2001) .Only now are these two approaches being married to delineate how form produces function. The impetus for this union has, again, arisen through experience with the repair of the mitral valve and the occasional need to manipulate the cords in order to alter the behaviour of the leaflets. The techniques of cordal transposition, division, and the insertion of artificial cords have now entered the clinical arena (Smedira et. al., 1996; Sousa et. al., 1993) .Once considered a homogenous entity providing support only in terms of preventing leaflet prolapse during ventricular systole, the cords may now be classified into broad groups according to the point of their attachment to the leaflets, and their attachment to the papillary muscles. Groups of cords sprout from both papillary muscles, and support the leading edges of both leaflets. Beneath the junctions of the primary and subsidiary zones of apposition of the leaflets are fan-shaped, or commissural, cords. It has been proposed that the location of such cords provides an identification of where one leaflet ends and another begins (Lam et. al., 1970a).The muscles themselves lie beneath the two ends of the primary zone of apposition between the leaflets, or beneath what has been called the commissures (Kumar et. al., 1995).This ensures a cordal supply to both leaflets from both muscles. Their destination on the leaflet provides the basis for classification (Lam et. al., 1970a) – free edge cords insert into the rough zone of the leaflet and ensure that the coapting surfaces meet during systolic closure. Strut cords are thicker than their free-edge counterparts, and are particularly frequent on the aortic leaflet. They insert at variable points on the ventricular aspect of the leaflet way from the rough zones. Basal cords are a third type of cord that do not take origin from the papillary muscles. They are the least frequent

variety and insert close to the annulus of the mural leaflet, and they are also only found only at the mural leaflet (Kumar et. al., 1995).The surgical trend has been to classify the free-edge cords as primary, or first-order, and secondary, or second order cords, as everything else. On occasion, however, basal cords have been assigned to the third order. This has led to an unnecessary amount of confusion, and that the credibility of such numerical systems of classification is undermined by their reliance on subjectivity. Contemporary studies on isolated hearts show that primary cords prevent prolapse of the leaflets (Obadia et. al., 1997).This is supported by the finding that rupture of these primary cords forms the basis for the unnatural history of acute mitral valvar regurgitation. The secondary cords, being more important in determining ventricular geometry and subsequent performance, may therefore be translocated surgically without compromising the distribution of cordal stress or coaptation of the leaflets (Smedira et. al., 1996).

In recent years, therefore, two main approaches to providing an understanding of the mitral valve, pure anatomical observation as opposed to surgical trial and error, have finally come together. The surgeon has once again become the anatomical pathologist, altering practice on the basis of what is seen and concluded in the operating room. What is now required is a standardization of methods and descriptions that will unite the surgeon with not only the morphologist but also the echocardiographer. We have to say what we mean before we can mean what we say! The problems faced in treating mitral valvar prolapse, and isolated cleft of the aortic leaflet of the mitral valve leaflet have brought issues of unity and clarity together.

Section 3.2: Growth changes in the normal mitral valve: bridging form and function

Introduction

Valve repair is the procedure of choice in the management of the incompetent mitral valve, especially in the paediatric setting where competence has to be secured without interfering with normal growth.

Although the basic morphology of the mitral valve is well described (Ho, 2002; Kanani et. al., 2003; Ranganathan et. al., 1970), little can be said for how the apparatus changes as the heart matures from the neonatal period to adulthood. Aside from increases in the length of the leaflet and annular dimensions, there are several obvious unresolved issues that may hold implications for the management of the congenitally incompetent valve, such as the pattern of leaflet growth, and how the arrangement of juvenile valve's subvalvar apparatus alters with time. In other words, could it be said that the paediatric valve is just a smaller, yet fully formed version of its adult counterpart? Furthermore, the surgical demands of a competent repair are driving a deeper understanding of not only the detailed anatomy of the heart, but how the individual anatomic components relate to each other in form and function. This is especially true of the valvar apparatus where dysfunction of one component may be enough to disrupt the entire system.

In this study, I will address some of these age and growth related changes of the mitral valve and advance the notion that, although the valve undergoes distinct changes in the rate of growth of individual valvar components as the heart matures, the adult arrangement has already established by postnatal life. I will also demonstrate that the subvalvar apparatus is arranged in such a manner as to provide the greatest support to the leaflet canopy for the given population of cords.

Materials and methods

Ninety-two normal hearts ranging from 2 weeks to 25 years old (mean 71.2 months, SD 65.6, median 50.5) from the Cardiac Registry of the Children's Hospital, Boston were examined with respect to the aortic leaflet of the mitral valve and the subvalvar apparatus. Each heart was examined in the following way:

1. Length of the aortic leaflet of the mitral valve from the annulus to the tip of the leaflet (Figure 3.5). The aortic leaflet was selected since it was easily measured, unlike the mural leaflet, which is more tethered to the ventricular wall to the extent that detailed analysis is impossible without avulsion.
2. Length of the rough zone of the aortic leaflet
3. Length of the anterior and posterior papillary muscles, from the base to the highest point of cordal origin.
4. Mean length of the tendinous cords of both papillary muscles, from their muscular origin to their point of insertion into the ventricular surface of the leaflet.
5. Total number of tendinous cords from both papillary muscles.
6. The pattern of division of the tendinous cords, and their geometric distribution into the ventricular surface of the aortic leaflet.

Figure 3.5 The aortic leaflet of the mitral valve from the aortic aspect. The leaflet is diided into the rough zone (RZ) that receives the tendinous cords beneath and the smooth zone (SZ) that is closest to the annulus. Courtesy of Robert H. Anderson

Statistical analysis

Continuous variables were expressed as a mean and standard deviation. Scattergrams were drawn for the each of the various ratios below in order to calculate the Pearson's correlation coefficient using StatView 4.57 (Abacus Concepts Inc., Berkley, CA).

Results

Cordal number

From the 90 hearts analysed, there was a mean number of 9 cords arising from both the anterior and posterior papillary muscles (range 6-14, SD 1.57, median 9).

Arrangement of the subvalvar apparatus

In all of the cases examined where the aortic leaflet was intact, there was consistency in the manner of arrangement of cordal insertion into the ventricular surface of the leaflet, with segregation to the rough zone. Although it could be seen that the cords had different destinations on the ventricular surface of the leaflet, it was observed that in many instances they were branches of the same cord arising from the apical portion of the papillary muscle. Thus, as the cord arose from the muscle, it usually divided into three successive generations that inserted progressively more deeply into the rough zone in an orderly manner. The first generation inserting into the free edge, the second generation into ventricular surface more towards the annulus, with the final, third generation, inserting into the ventricular aspect as the thick strut cord (Figure 3.6). Cords were also seen to insert directly intro the leaflet without division, but these

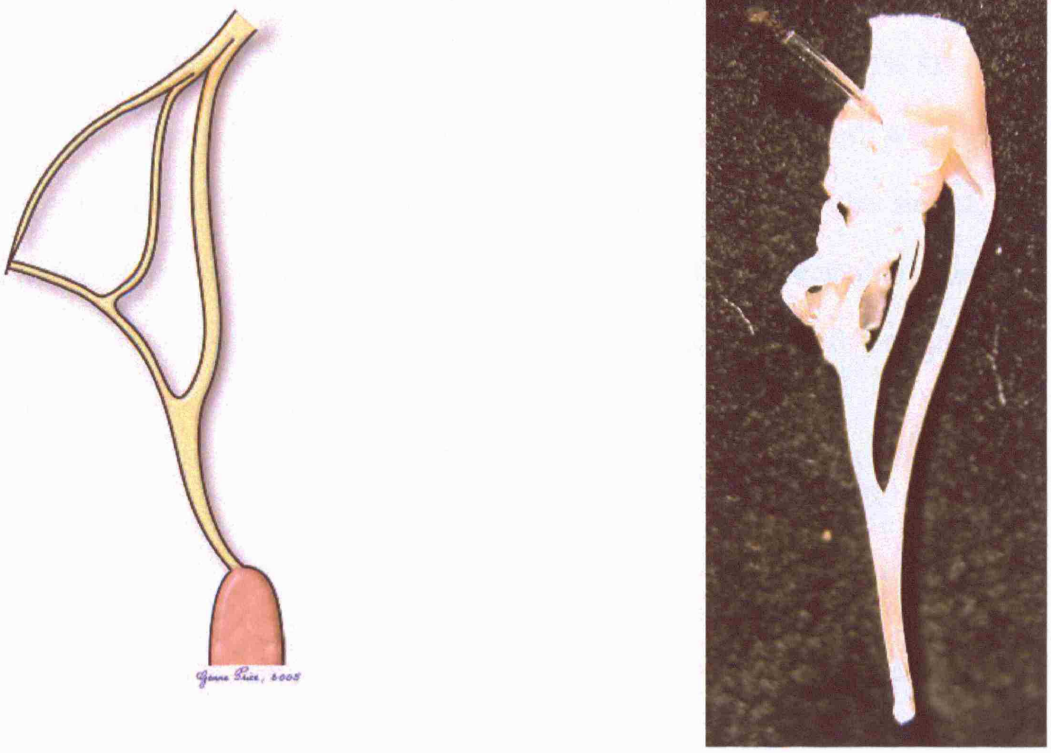

Figure 3.6 The principle cord arising from the papillary muscle divides into free-edge and strut cord elements. This arrangement allows the cord to support the entire length of the leaflet from annulus to free-edge. The arrangement also gives the underside of the leaflet a plate-like arrangement composed of three laminae. See also Figure 3.13

formed a significantly smaller population of cords with a median of only 26.68%, SD 10.47 of the total cords compared to those dividing thrice; median 54.71% SD 16.33, $p<0.001$) – Figure 3.7 The most common population of undivided cords were the fan-shaped cords that supported the so- called commissure, located on either side of the line of coaptation between the aortic and mural leaflets. These specialized population of cords were only ever seen to divide along the free edge of the leaflet, and never into the ventricular surface towards the annulus.

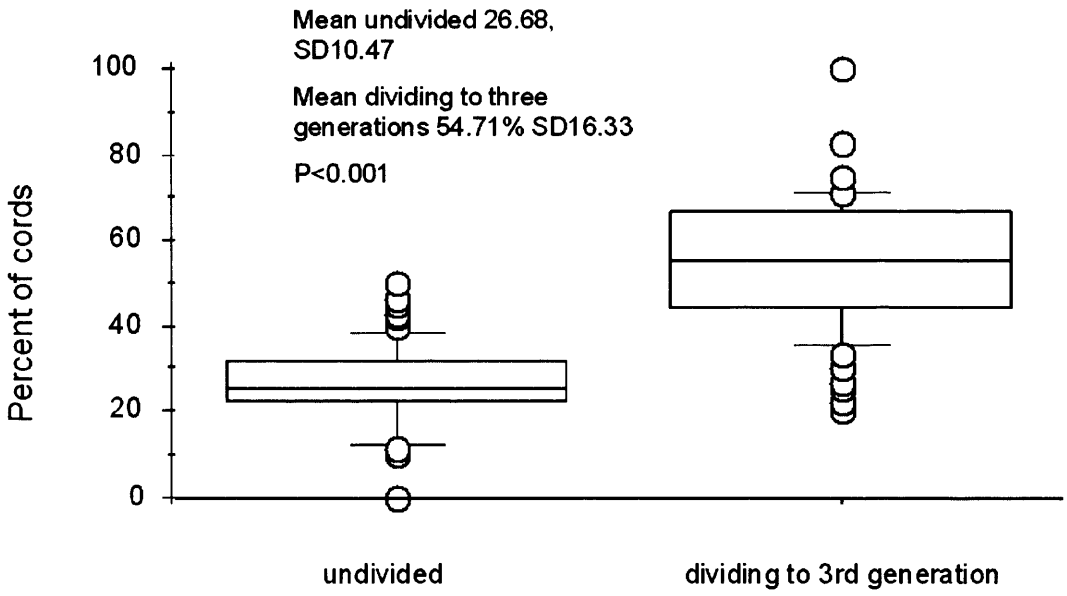

Figure 3.7 Box and whisker plots demonstrating that within the arrangement of the subvalvar apparatus, a significant proportion of tendinous cords arising from the papillary muscle divide into three generations compared to those that arise from muscle without dividing further

Thus, the pattern of cordal division and insertion was found to influence the organization of the ventricular surface of the aortic leaflet itself, giving it a distinctive appearance that was consistent across all age ranges examined. At the point of insertion, the cord was seen to broaden and blend with the leaflet. Given that there were a maximum of three generations of division for each cord arising from the papillary muscle, the combination of broadening and layered cordal insertion gave the ventricular surface the appearance of consisting of three laminae or plates stacked atop each other, with each lamina being continuous with the expanded distal ends of the cords (Figure 3.8)

Figure 3.8 The overall cordal arrangement at the ventricular aspect of the aortic leaflet. With laminar plate formation owing to the pattern of division of cords with broadening of their distal ends to blend with the leaflet. The right hand panel shows a closer view of this arrangement in another specimen. As the leaflet canopy opens, the laminae separate from one another

Pattern of cordal division and insertion

In all of the hearts examined, it was seen that the ventricular surface of the aortic leaflet was composed of these three laminar plates stacked atop each other. This unchanging arrangement is indicated by the scattergrams in Figure 3.9 that show a lack of relationship between the degree of cordal division and the age of the heart. For the number of undivided cords, correlation coefficient = -0.11, P = 0.91, for the number of cords dividing to the 3rd generation, correlation coefficient = -.033, P = 0.058

Changes in the Rough zone and leaflet lengths with age

Figure 3.10 demonstrates a significant reduction of the length of the rough zone to total leaflet length with increasing age (correlation coefficient = -0.45, $p<0.0001$) despite an overall increase in length of both variables with time

Age-related changes in the papillary muscle cord length ratios

There was a progressive reduction in the ratio of the length of the anterior and posterior papillary muscle compared to their respective tendinous cords. Figure 3.11shows the scattergram for the anterior (correlation coefficient = -0.33, P = 0.017) and posterior (correlation coefficient = - 0.30, P = 0.047)

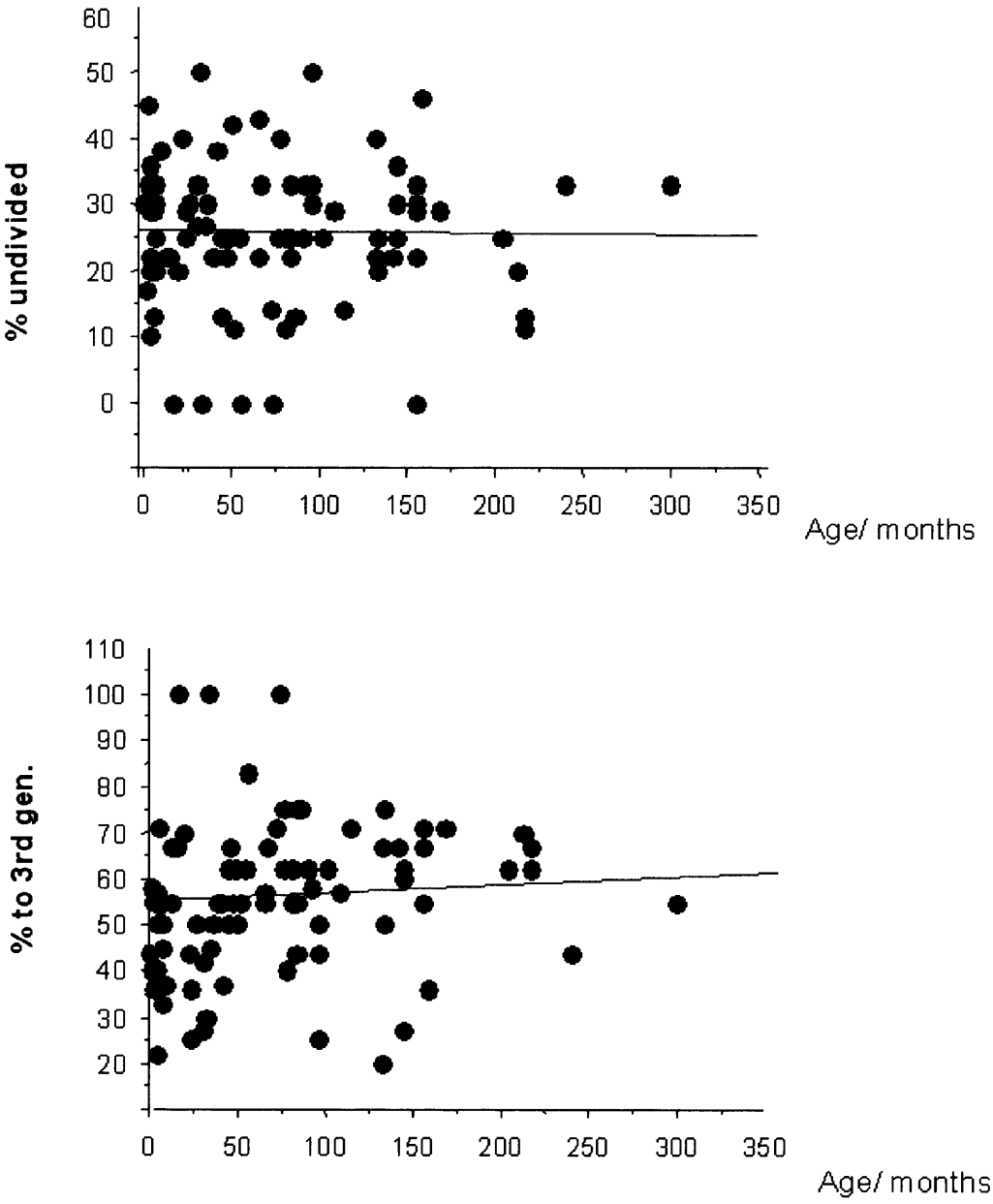

Figure 3.9 Scattergrams demonstrating the relationship between the percentage of undivided cords in the normal mitral valve and the age of the heart in months. The top figure demonstrates no relationship between the age of the heart and the percentage of undivided cords found at the aortic leaflet (Correlation coefficient= -0.11, P = 0.91). Similarly, there is a lack of relationship between the number of cords dividing into 3 generations and the age of the heart, lower panel (Correlation coefficient = 0.20, P = 0.058)

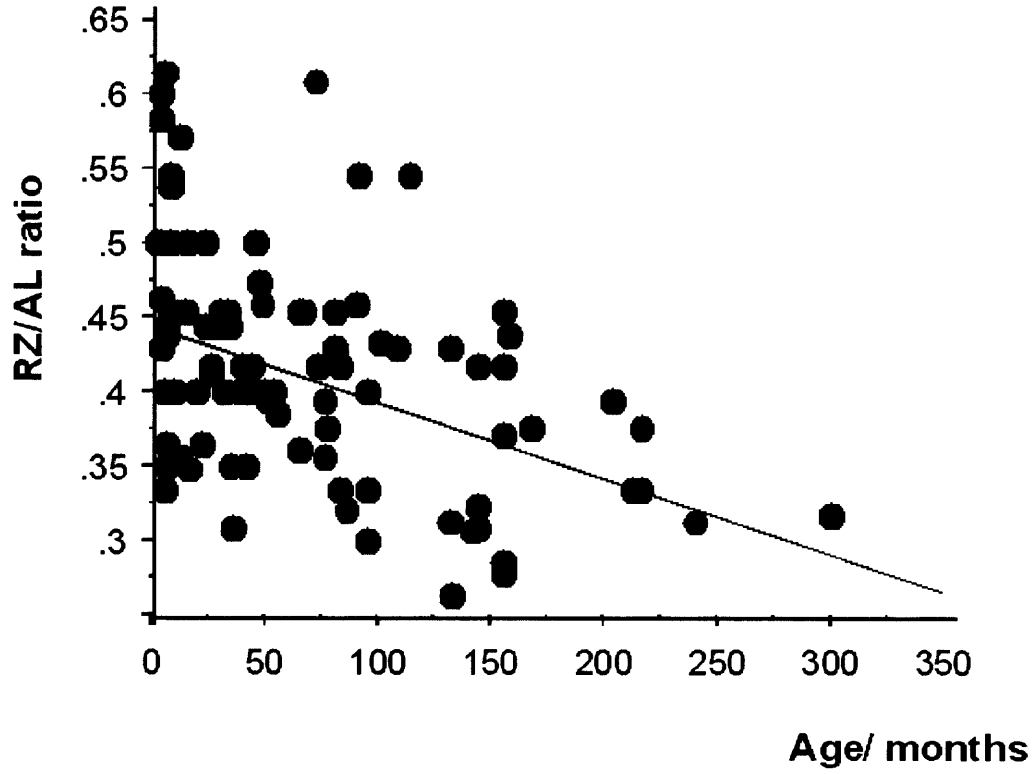

Figure 3.10 A scattergram demonstrating the relationship between the ratio of the RZ length to total aortic leaflet length (AL) and the age of the heart. There is a significant reduction of this ratio with age, suggesting that the first part of the aortic leaflet to grow is the RZ, with all subsequent growth being from the SZ

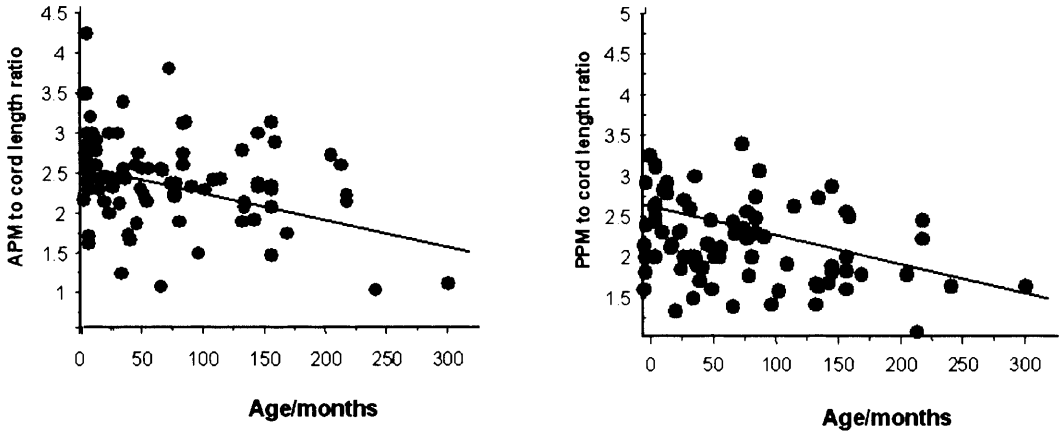

Figure 3.11 Scattergrams demonstrating how the relationship of the ratio of the anterior (left panel) and posterior (right panel) papillary muscle lengths to the lengths of their respective tendinous cords changes with the age of the heart. In both instances, there is a significant relative increase in cordal length with time. For the anterior muscle, correlation coefficient = -0.33, P= 0.017. For the posterior muscle, correlation coefficient = 0.30, P = 0.047

Discussion

Three types of tendinous cords are recognised – free edge cords that insert into the edge of the leaflet, strut cords that insert into the ventricular surface, and finally, the basal cords that originate from the ventricular wall and insert into the ventricular surface of the mural leaflet close to the annulus (Lam et. al., 1970a). Although it is known that the free-edge cords, synonymous with marginal or first order cords, are vital to leaflet coaptation, there has been recent interest in the "strut" or "stay cords" that have been likened to thick cables that hold the mast under any point of sailing (Duran, 2002). It has previously been observed that there are up to four such cords at the ventricular surface oft the leaflet (Rijk-Zwikker et. al., 1994), each being vital to the maintenance of left ventricular geometry and global function (Obadia et. al., 1997), with deleterious effects to systolic function if divided (Nielsen et. al., 2003) without affecting leaflet coaptation and valvar competence (Timek et. al., 2001).

Thus, although cords have been well described with respect to their final destination into the leaflet (Lam et. al., 1970), and the physiologic properties of each type of cords have been analysed closely (Chen et. al., 2004; Liao et. al., 2003; Nielsen et. al., 2003), I have shown that, in fact, they usually take origin from the same principle cord at the papillary muscle. I contend that the thick strut cord is a direct and linear continuation of this principle cord, consistent with previous observations (He et. al., 2000), but that crucially, the marginal branch often arises from this thicker cord, but at a more acute angle enabling it to reach the edge of the leaflet. Thus, although these two cordal forms could not be any more different in their, size, position and function, more often than not, they arise from the same "parent" cord from the papillary muscle. Furthermore, once generated, these cords insert into the ventricular surface of the leaflet radially, broadening at their distal end to blend into the leaflet, giving it a layered appearance.

This radial and laminar arrangement conferred to the leaflet by the manner of its cordal insertion may have been noted by da Vinci in the 16th century (O'Malley et. al., 1952) but to our knowledge, has not been described in the modern literature (Figure 3.12). The only cords that consistently do not show this pattern are the fan-shaped cords that support the so-called commissural areas located on either side of the zone of apposition between the two leaflets (Lam et. al., 1970). The observation of common cordal origins, together with confirmation of an organised and layered arrangement to the leaflet, emphasises the notion that the components of the valve work as an integrated functional unit, and that altering the form of one component may compromise the function of another.

Figure 3.12 Cartoon by Leonardo da Vinci from circa 1513, which may show the laminated appearance of the ventricular surface of the aortic leaflet of the mitral valve. This concept has, to our knowledge, never been reproduced in the modern literature (from O'Malley and Saunders 1952)

This begs the question about the physiologic consequences of this laminar arrangement of the aortic leaflet. Conceivably, it may permit the greatest and most efficient support for any given population of cords. Thus, each cord from the papillary muscle, through generational division, may support the entire length of the leaflet from annulus to coapting edge, with a more even distribution of tensile strength along the leaflet canopy (Figures 3.6 and 3.13). The radial arrangement of the layered insertion may also aid in evenly distributing forces across the canopy area, limiting load burden on any individual area. For this reason, in terms of function, cords must not be considered in terms of isolated sub- types, as previously held in the anatomic perspective, but rather that each cord must be considered as an integrated unit consisting of strut and free-edge components within a greater organization at the ventricular surface of the leaflet. It can be seen that this basic arrangement has already been established by postnatal life and persists into adulthood.

Leaflets consist of rigid fibrous material with little inherent ability to stretch. Despite this, the leaflets are required to form a competent and flexible canopy that can cope with a regurgitant jet beneath. The layered nature of the leaflet so conferred may permit the leaflet to attain a level of flexibility and extensibility that a uni-layered sheet does not permit. As the force beneath the leaflet increases, the laminar plates separate, causing the leaflet to arch and canopy, with the force being directed down a single cord from its branches (Figure 3.13), with the free-edge branch supporting the leaflet edge, and the strut component holding steady the line between the papillary muscle and annulus. All of these physiologic contentions are, of course, presently conjecture in the absence of in-vivo experimentation, but conceivable in the light of these observations and what we know of the physiology so far.

Figure 3.13 Schematic illustrations demonstrating how the laminar arrangement of the aortic leaflet may aid in the flexibility of a leaflet composed of rigid material. As the regurgitant jet hits leaflet from below (right hand panel) that laminae separate allowing the leaflet to pull forward. Owing to the generational division of the principle cord from the papillary muscle, the line of tension is directed down the thick cord and down the axis of the papillary muscle. Thus, a single cord can support the entire length of leaflet from annulus to free-edge. See also Figure 3.6

The study also suggests that as the valve matures, the rough zone, and therefore the coapting surface, becomes relatively narrower. This implies that the postnatal growth of the leaflet occurs from the annular margin, a notion that it entirely consistent with previous observations in the developing heart demonstrating that the rough zone develops first, in close association with the subvalvar apparatus(Lamers et. al., 1995; Wenink et. al., 1986). Likewise, as the valve increases in size, the cords elongate at a greater rate than the papillary muscles as suggested by a significant reduction in the papillary muscle to cord length ratio. This changing relationship may have to bourne in mind during surgical repair of the mitral valve at different ages, especially during cordal manipulation or when sizing artificial cords. Nevertheless, despite these different rates of growth for individual components of the valve, it must be emphasised that the anatomic organization that defines the relationships of the cords to the leaflet have already been set by post natal life, thus integrating the function of the different cordal types from the outset.

Section 3.3: The arrangement of the mitral commissures

Introduction

The commissures of the mitral valve have traditionally been defined as the common points on the annulus where the aortic and mural leaflets meet. However, remaining faithful to the strictest sense of the word, the term "commissure" should be reserved for the entire line of coaptation between the aortic and mural leaflets, and not merely the locii at either end.

These two areas, that are set some 5mm away from the annular ring (Ho, 2002), are supported by their own population of specialized fan-shaped tendinous cord that differ in their morphology to those of the remaining leaflet skirt. Specifically, a solitary tendinous cord arising from the apical region of its respective papillary muscle, arborises into a network of smaller branches that insert along the entire edge, and in doing so, support theses two corners at either side of the line of coaptation. As each cordal branch approaches the edge, it broadens and blends with the leaflet substance. These fan-shaped cords are segregated to the leaflet edge, and do not insert into the ventricular surface of the leaflets (Lam et. al., 1970a) Although this arrangement is well known, it begs the question as why the commissures require this singular arrangement of cordal support, and what benefits it confers to valvar competence. Understanding of the support principles at this region will also allow the understanding of how the zone of apposition between the left ventricular portions of the bridging leaflets in atrioventricular septal defects, often compared to the mitral commissures, deviates from this "Gold-Standard" of commissural support seen in the normal heart.

Methods and results

Ninety-two normal mitral valves were examined from the collection at the Cardiac Registry of the Children's Hospital, Boston in order to determine the variability in the pattern of cordal support at the so-called commissures, and in doing so, demonstrate that this fan-shaped arrangement is ideally suited to the physiologic needs of this region of the leaflet skirt. In all of the hearts examined, it was seen that these cords, found arising from the apex of a single muscular peak of the papillary muscles usually divided into smaller branches that blended with the leaflet edge. This arrangement was consistent irrespective of which papillary muscle the cords arose from, and size of the heart. Examining the ventricular surface of the commissure, confirmed that unlike the rest of the leaflets, the fan-shaped cords of the commissure divided only along the length of the leaflet without giving branches to the ventricular surface. An illustrative study was made of twelve such commissural cords, demonstrating the variability in the pattern of division of the commissural cords along the length of the aortic and mural leaflets (Figures 3.14 and 3.15)

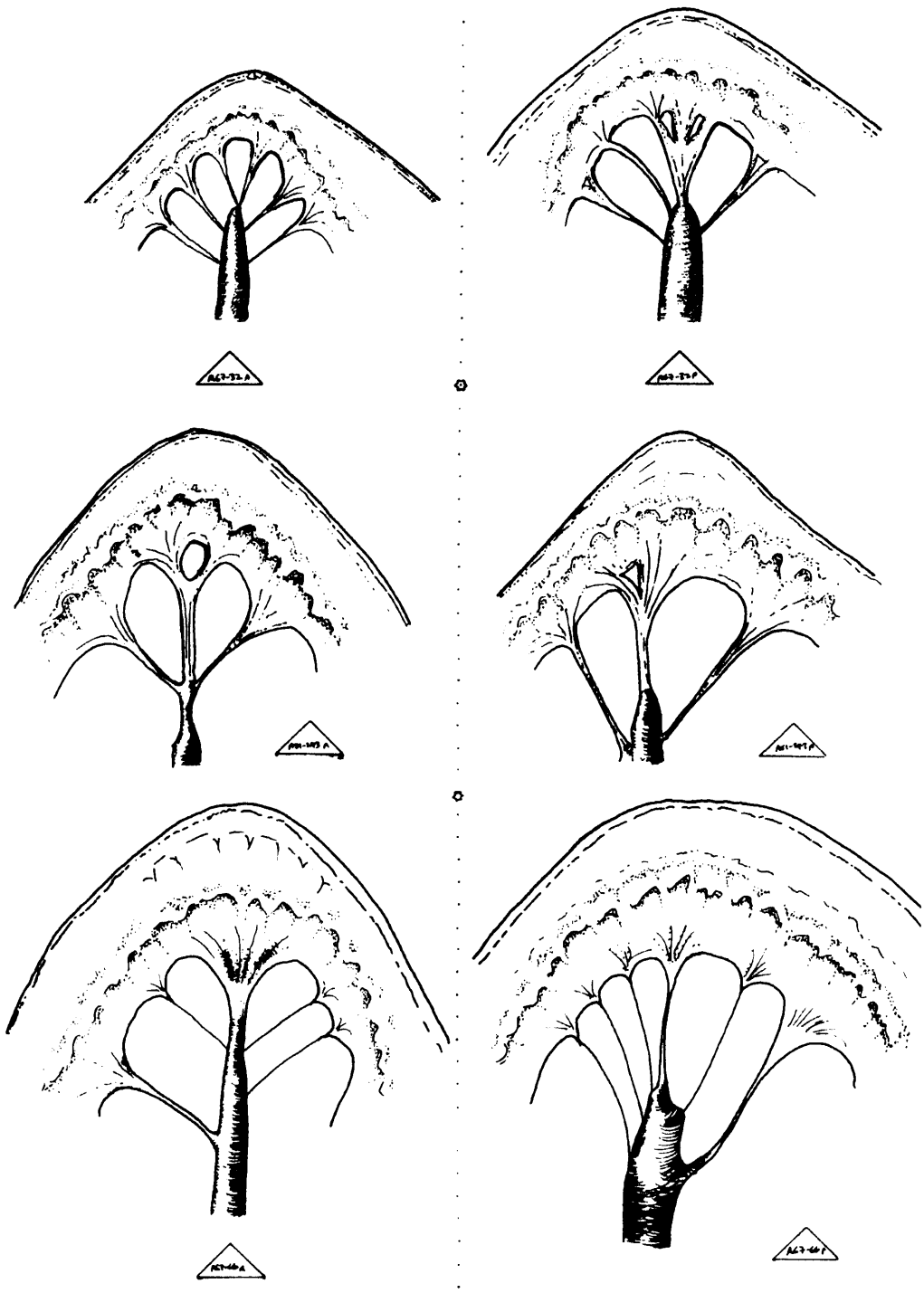

Figure 3.14 The arrangement of the cordal support at the so-called commissures of the normal mitral valve, showing that the entire length of the commissural corner between the aortic and mural leaflets is supported by a single fan-shaped cord

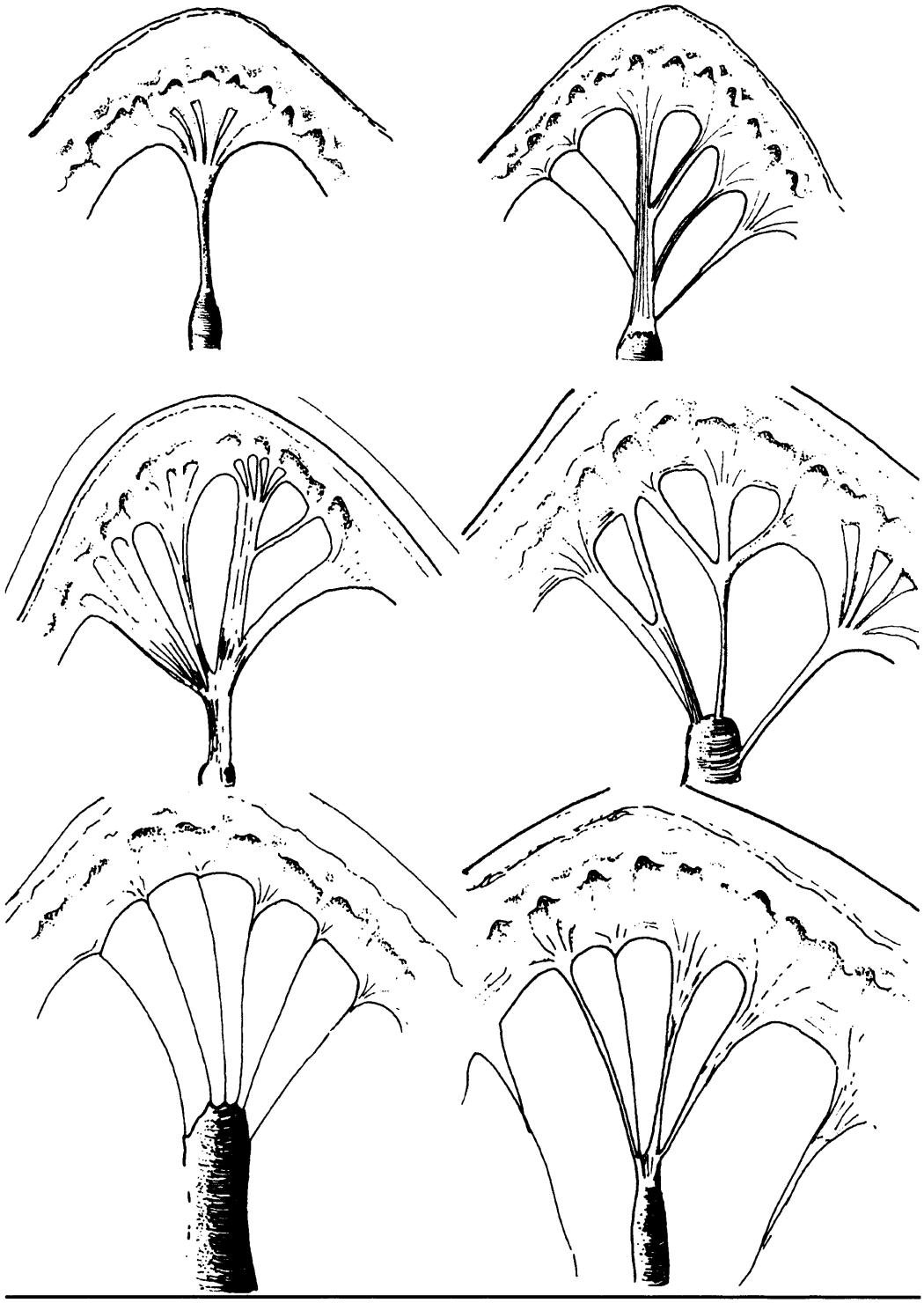

Figure 3.15 Further illustrations of the commissural cords. Despite great variability in the pattern of cordal division and number, the principle organization is adhered to.

Although all of the cords at the commissure could be classified as "fan-shaped", owing to their characteristically distal broadening, their individual morphologies were highly variable. Several types of morphology were seen

1. Multiple cords arising individually from either side of a long and thin muscular peak
2. As a single cord arising from the peak of a papillary muscle. The single branch broadens into several diverging cords. The tissue between the cords is in various states of fenestration so that the cords may be seen an individual branches, or otherwise as a single fanning sheet from the distal end of the principle cord.
3. As a single cord arising from the peak of a papillary muscle. This principle cord is short and thick, and divides into multiple fan-shaped cords soon after arising from the papillary muscle.

Among these types of pattern, there was great variability in the lengths of the tendinous cord, pattern of division, and the degree to which the distal end broadened.

Discussion

The two loci at either end of the line of coaptation between the aortic and mural leaflets, termed colloquially the "commissures" are important to consider anatomically and functionally for a number of reasons. Since it is the location of a natural transition from one leaflet to another, it is a potential "Achilles' heel" in the valvar apparatus. Similarly, the edge of the valvar leaflet at these corners are positioned some 5mm from of the annulus, rendering it the least mobile part of the mitral leaflet apparatus. Furthermore, understanding the physiologic role that these loci play in the overall

attainment of valvar competence may hold implications for the management of the zone of apposition between the left ventricular components of the bridging leaflets in atrioventricular septal defects, an area often compared to the mitral "commissures." The importance of this comparison will be discussed in subsequent chapters

Although there is great variability in the patterns seen, they all conform to one essential arrangement – where all of the free edge cords converge on to a larger cord that arises from the apex of its respective papillary muscle or onto the apex of the papillary muscle itself. Thus, during ventricular systole, when the tension on the mitral sub-valvar apparatus is at its greatest, all of the tension on the free-edge cords is directed towards this common point. This provides the maximum support for the given population and permits the even distribution of support along the entire length of the so-called commissural area (Figure 3.16).

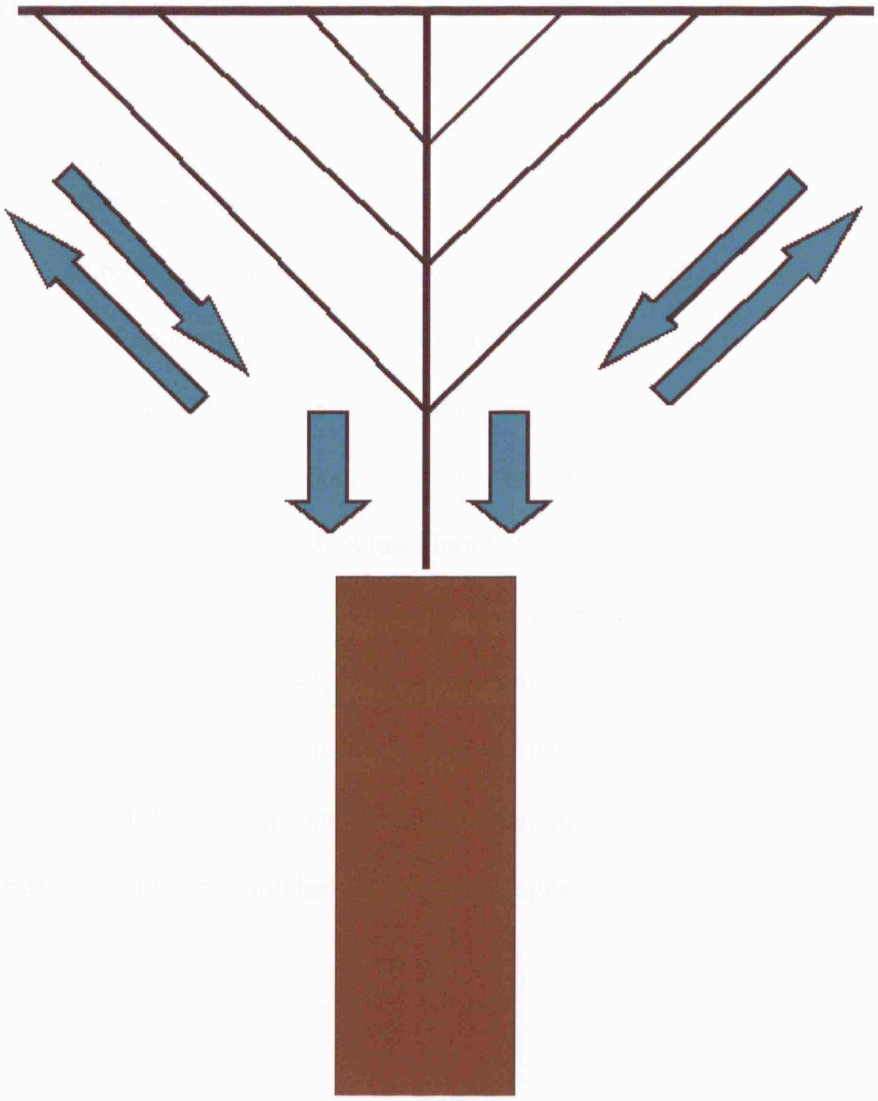

Figure 3.16 Schematic representation of the cordal arrangement at the so—called commissures of the mitral valve. Although there is great variability in the pattern of free-edge cords, in all cases examined, these free-edge cords are connected to a single cords that arises in line with the papillary muscle. The arrows represent the direction of tension which passes down this cord, in the axis of the papillary muscle. Thus, a single cord may support an entire length of commissure

Executive Summary

In this chapter, the anatomy of the mitral valve has been introduced, enabling it to be placed in a position that will permit a reasonable contrast with the left atrioventricular valve in atrioventricular septal defects. One can consider the mitral valve to be the "Gold-standard" for efficiency of the subvalvar support mechanism. As has been demonstrated, each component of this system, whether the ordinary cords, or the specialized cords of the commissural area adheres to a structural principle that demonstrates remarkable consistency between individual hearts. We have also seen that by and large, this organization has already formed by early post-natal life and persists in to adulthood. It follows that any sub-valvar arrangement that veers from this standard is placed at a structural disadvantage, laying the foundations for early or late valvar incompetence. I will go onto show that hearts with deficient atrioventricular septation fall short of these normal standards, and that this subvalvar abnormality and deviation from normal mitral morphology persists despite surgical repair.

Chapter 4: The detailed morphology of the zone of apposition in atrioventricular septal defect with common atrioventricular junction

Introduction

Although there are many facets to the surgical repair of atrioventricular septal defects, central to the issue is the management of the zone of apposition between the left ventricular aspect of the bridging leaflets. Knowing that it is the Achilles' heel of surgical repair has long provided the impetus to the definition of its structure, and hence, contribution to the competence mechanism of the left atrioventricular valve. Investigators have understood that if it were known what this zone represented morphologically, it could permit the surgeon to correct the defect and restore the intended arrangement. Thus, if it is an unsupported, morphologic flaw in the aortic leaflet, it may be closed directly in order to restore the normal anatomy, as in the case of the so-called isolated cleft of the mitral valve. If it is analogous to the so-called commissures of the mitral valve, the junctions between the aortic and mural leaflets, it may be repaired as such, preserving the valve's native tri-leaflet arrangement.

In the detailed study of the left atrioventricular valve we will demonstrate that unlike the case of the normal mitral valve, where the morphologic principles of design are highly conserved among different hearts, in atrioventricular septal defect, valvar morphology is characterized by heterogeneity at all levels. These differences may explain the variability in pre-operative valvar competence, with implications for the long-term outlook following repair.

Materials and Methods

Two-hundred and two hearts with atrioventricular septal defect with common atrioventricular junction were examined from the collections at Great Ormond Street Hospital Cardiac Archive (124 hearts), The Frank E. Sherman, Cora C. Lenox Heart Museum, Children's Hospital of Pittsburgh, PA (43 hearts) and the Cardiac Registry, Children's Hospital, Boston, MA (35 hearts). Eighty-four hearts were excluded immediately for the following reasons:

- Damage to the leaflets
- Damage to the subvalvar apparatus
- Previous surgery to the bridging leaflets that distorted the anatomy of the zone of apposition
- Presence of isomerism of the atrial appendages

This left 118 specimens, 77 with a common valvar orifice, and 41 with separate valvar orifices. These hearts were subjected to the following, detailed examination of the zone of apposition between the bridging leaflets:

- The morphology of the coapting surface between the bridging leaflets and how the morphology varied between types of atrioventricular septal defect.
- The source and pattern of cordal support to the zone of apposition.
- The arrangement of the cordal support to the subvalvar surface of the bridging leaflets.

Statistical analysis

Cordal division was expressed as the median percentage and range. To test for significant differences in the percentage of cords dividing to three generations or remaining undivided, and Mann-Whitney U test was performed, an the p value expressed at the 95% confidence interval

Results

Morphology of the coapting surfaces

With a common valvar orifice

In all of the cases of atrioventricular septal defect with a common valvar orifice, the edges of the superior and inferior bridging leaflets were folded at the zone of apposition to form the coapting surface, reminiscent of the coapting surface between the aortic and mural leaflets of the mitral valve (Figures 4.1a and b). This folded surface was the thinnest and most pliable part of the leaflet. Unlike the coapting surfaces in the mitral valve, at the zone of apposition, the coapting surface was not smooth. The portion closest to and overlying the crest of the ventricular septum was usually found to be nodular and irregular. Such nodularity was identified as the so-called kissing point of the valve, often identified by the surgeon at operation in order to align the leaflets prior to closure of the zone of apposition (Figure 4.2). It was usually the case that the larger the heart, the greater the irregularity of this coapting edge to the point of frank dysplasia.

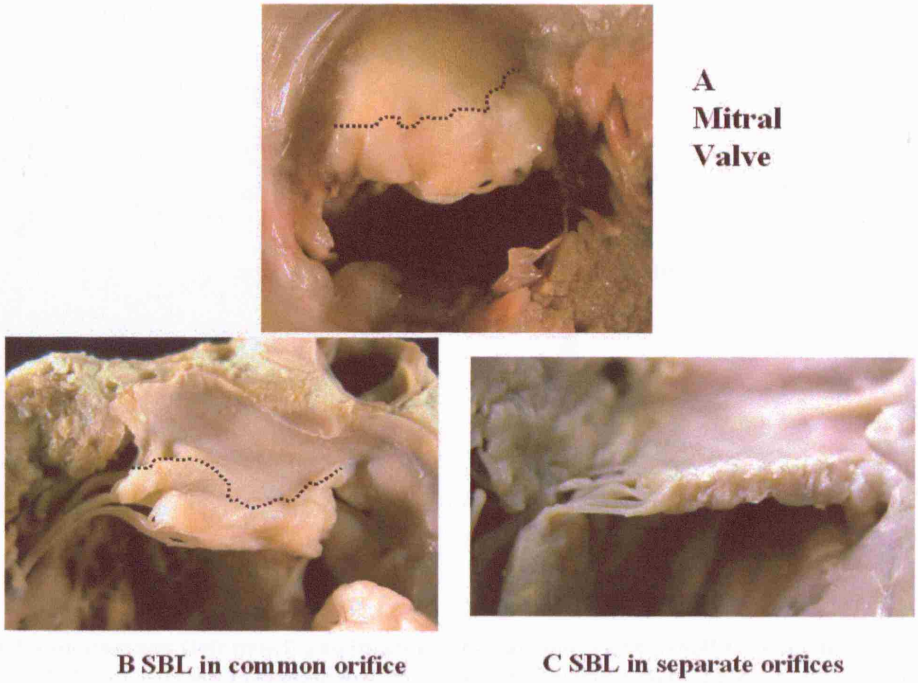

Figure 4.1 Photographs of the aortic leaflet of the mitral valve (Panel A), superior bridging leaflet (SBL) in common orifice AVSD (Panel B) and superior bridging leaflet in separate orifices AVSD (Panel C). In both the mitral valve and the SBL of the common orifice defect, the free edge of the leaflet is folded to form a coapting edge (dotted line). This allows the leaflet to canopy and adds to the competence mechanism. In the defect with separate orifices, the SBL forms a plate-like coapting edge

With separate valvar orifices

In all of the hearts examined with separate orifices, save four specimens, the coapting surface at the zone of apposition was not formed by a terminal folding of the leaflet. Instead, the surface was formed from a thickening of the leaflet edge, giving the zone the appearance of two plates coming together (Figure 4.1c). In smaller hearts, the surface of these plates of leaflet tissue was smooth and uniform. In larger hearts, even with a greater degree of thickening and dysplasia at the edge, specific valvar "kissing points" could not be identified between the bridging leaflets. In 29 out of the 41 hearts with separate orifices examined, the zone of apposition did not extend to the crest of the ventricular septum, but to its left ventricular side depending on the ambit of the connecting tongue.

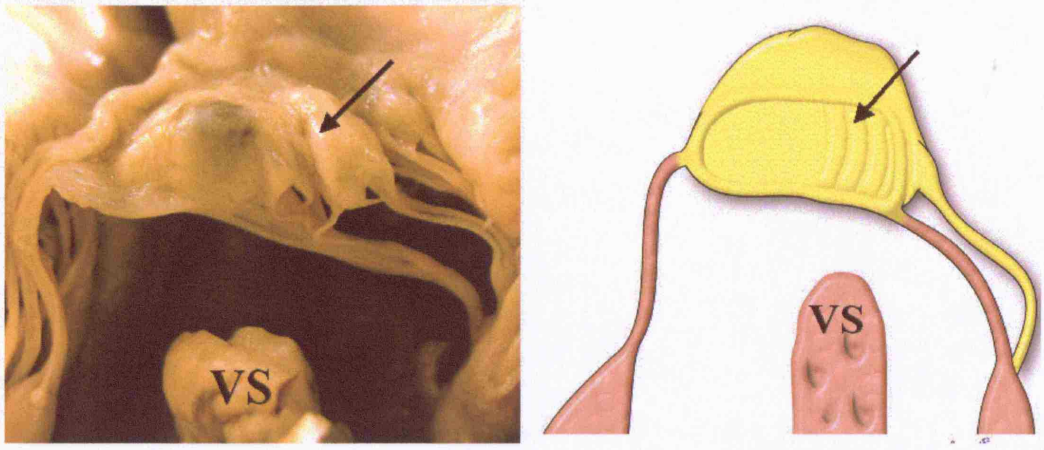

Figure 4.2 a photograph (left panel) and its schematic cartoon (right panel) showing the superior bridging leaflet in AVSD with common orifice in the four-chamber view. This is a Rastelli Class C defect, with extreme bridging of the SBL across the ventricular septum (VS) into the right ventricle. Its zone of apposition is well supplied by cords from both the papillary muscles of the left and right ventricles. The black arrow marks the position of the so-called kissing point of the valve, where the corrugated edge meets with its counterpart on the inferior bridging leaflet. This area is also well supplied by tendinous cords

Cordal support to the coapting surface

There were found to be three potential sources of cords to the zone of apposition; consistently from the left ventricular papillary muscles; variably from either the ventricular septum, and/or from the medial papillary muscle of the right ventricle. The degree of involvement of these three structures depended on whether there were separate or common orifices, and on the degree of bridging of the leaflets.

With a common valvar orifice

In the so-called Rastelli type A variety, with minimal bridging of the superior bridging leaflet into the right ventricle, the zone of apposition very well supported by cords from the crest of the ventricular septum (Figure 4.3). These cords were primary, going to the edge of the coapting surface; or secondary, inserting into the ventricular surface of the leaflet. In 8 out of the 39 cases of type A leaflet, these septal cords were distributed along the entire length of the zone of apposition on the superior bridging leaflet side. This cordal morphology showed a continuum from those that were thin, long and pliable, to those that were thick and dysplastic. This variability was independent of the size of the heart.

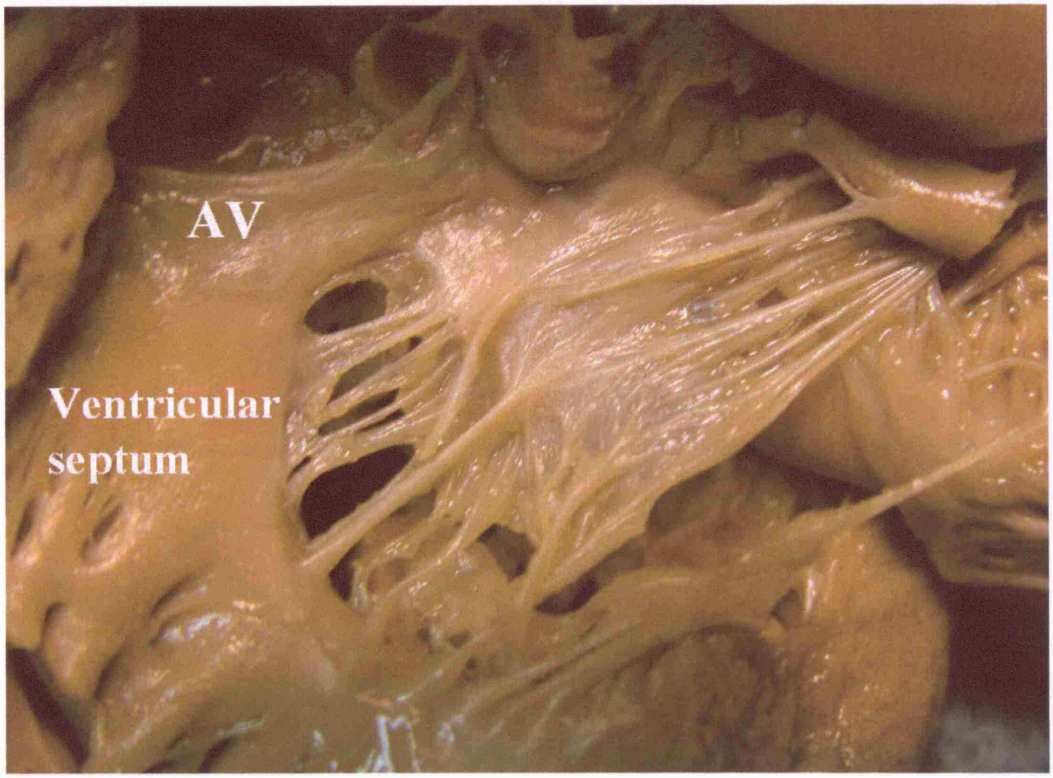

Figure 4.3 Photograph of the ventricular surface of the SBL in the Rastelli Class A defect, looking towards the left ventricular outflow tract and aortic valve (AV). The SBL is supplied from both the superior papillary muscle of the left ventricle and the crest of the ventricle septum. Multiple intercordal spaces permits shunting at the ventricular level. Despite this abundant supply, cords insert into the leaflet in a disorganized and haphazard fashion

In twenty-three out of the 39 (59%) hearts with the type A arrangement, cords at the leaflet edge were found to form part of the coapting surface (Figure 4.4). In these situations, fused cords at the leaflet edge formed a sheet extending from the septal crest to the leaflet, consequently forming the inferior portion of the coapting surface. In these situations it was sometimes difficult to identify the boundary between leaflet and cord.

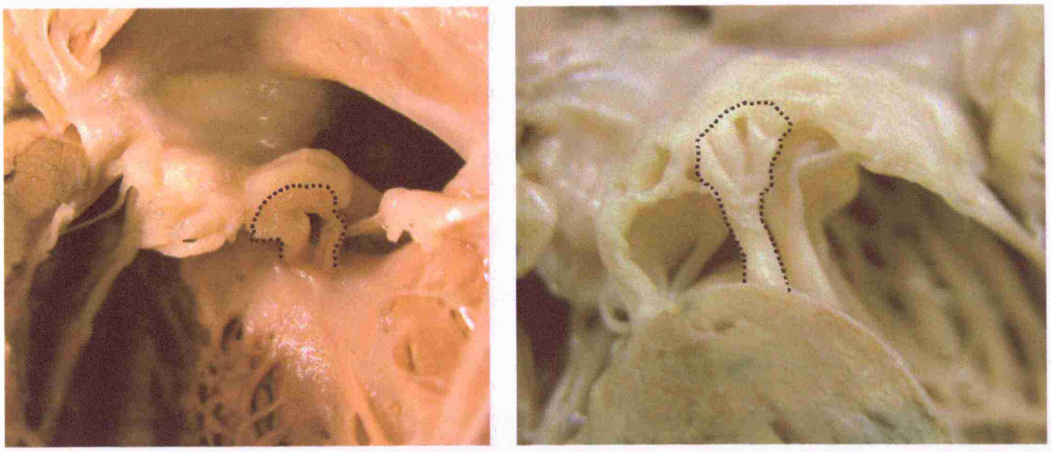

Figure 4.4 Photograph of the SBL in the Rastelli class A defect where there is cordal supply from the crest of the ventricular septum. In these examples, the dysplastic cords are flattened to form part of the coapting surface (marked by the dotted line) at the zone of apposition with the IBL. This is not seen in the mitral valve.

At the other extreme were the hearts with the Rastelli-type C arrangement to the superior bridging leaflet, where the leaflet straddles the crest of the ventricular septum between right and left ventricular papillary muscles. In all cases, the cordal supply was segregated to the left and right ventricular ends of the coapting surface of the superior bridging leaflet. Anteriorly, cords came from the superior papillary muscle; posteriorly from the medial papillary muscle of the right ventricle. These posterior cords were found to be concentrated beneath the kissing point of the zone of apposition (Figure 4.2). In this arrangement, owing to the lack of cordal support from the crest of the ventricular septum, cords did not form part of the coapting surface, unlike in some cases of the Type A defect.

The cordal supply to the inferior bridging leaflet side of the zone of apposition in hearts with a common valvar orifice were a lot more plentiful. The inferior bridging leaflet was always found to be tethered to the crest of the ventricular septum with tendinous cords, irrespective of its degree of bridging into the right ventricle (Figure

4.5). No relationship was found between the degree of bridging of the superior and inferior bridging leaflets. In 54 out of the 77 (70.1%) hearts with a common orifice, collections of fused cords over the septal edge of the zone of apposition at the inferior bridging leaflet were involved in forming the coapting surface. In 29 out of the 77 (37.6%), the inferior bridging leaflet side of the zone of apposition was supported along its entire length by cords from the inferior bridging leaflet and ventricular septum.

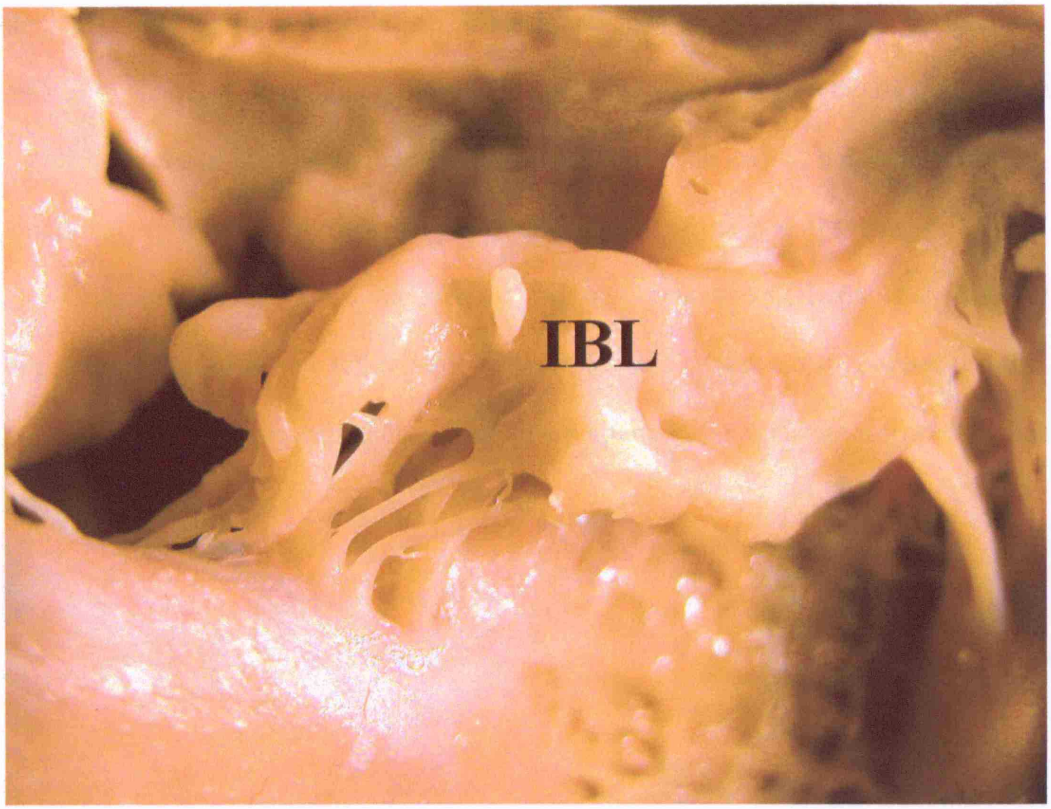

Figure 4.5 Photograph of the inferior bridging leaflet (IBL) in AVSD with a common orifice, looking towards the left ventricular side of the ventricular septum. It is tethered to the ventricular septum by numerous tendinous cords that insert into the base of its zone of apposition with the SBL

With separate valvar orifices

The cordal support was generally more deficient than the defect with the common orifice, independent of the size of the heart. In 36 out of the 41 (87.8%) cases observed, there was no cordal supply to either side of the plate-like zone of apposition, from either the papillary muscles, or the ventricular septum (Figures 4.1c & 4.6). When present, septal cords were thicker, shorter and difficult to distinguish from leaflet material. Beneath the bridging leaflets, cords from the papillary muscles were fused to the leaflet, giving the ventricular surface a ribbed appearance, running along the long axis of the leaflet from papillary muscle to ventricular septum. In 6 hearts, there was no identifiable cordal support to the ventricular surface of the leaflet, being uniformly smooth along its entire surface. This was independent of the size of the heart.

Among 32 specimens, the inferior bridging leaflet was deficient at the zone of apposition, with extensive tethering to the ventricular septal crest. In these cases, the zone of apposition was angled away from the perpendicular axis demonstrated by hearts with common orifices.

Figure 4.6 Photograph of the ventricular surfaces of the bridging leaflets in AVSD with separate orifices, looking from beneath. The green star indicates the position of the ventricular septum. The dysplastic cords are fused to the ventricular surfaces of both leaflets, producing a corrugated appearance to the ventricular side of the leaflets. Again, the Zone of Apposition is unsupported along its entire length. SBL, superior bridging leaflet; IBL, inferior bridging leaflet.

Pattern of cordal division

Figures 4.7 & 4.8 are box and whisker plots of the pattern of cordal division for defects with common and separate orifices. For defects with a common valvar orifice, a median of 15.5% of superior bridging leaflet cords divided to the third generation (range 0-75%), compared to a median of 6.4% for defects with separate orifices (0-30%). The difference between the two types of defect was statistically significant, $p = 0.036$.

Similarly, there were a significantly greater proportion of undivided cords in hearts with a separate orifice (median, 71.0%; range 25-100%) compared to defects with a common orifice (median, 55.5%; range 10-100%), p = 0.04 (Figure 4.8)

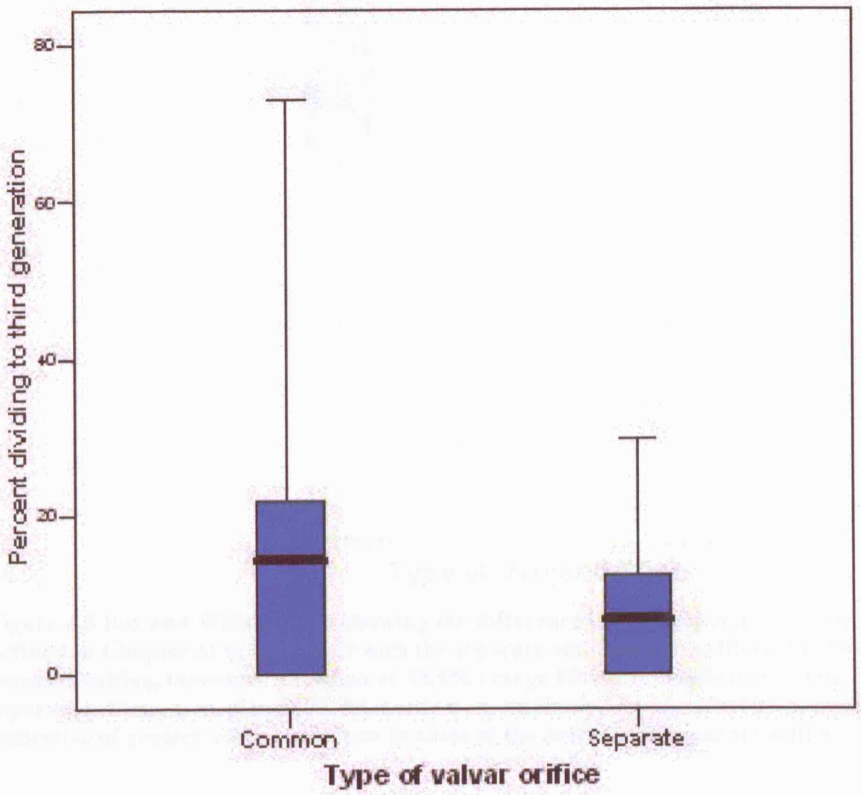

Figure 4.7 Box and Whisker plot showing the difference in the proportion of cords dividing to the third generation (as defined in Chapter 3) in the defect with the separate and common orifices. In the common orifice defect, a median of 15.5% of cords (range 0-75%) divide into the third generation, compared to 6.4% (range 0=30%) of defects with separate orifices, p = 0.036

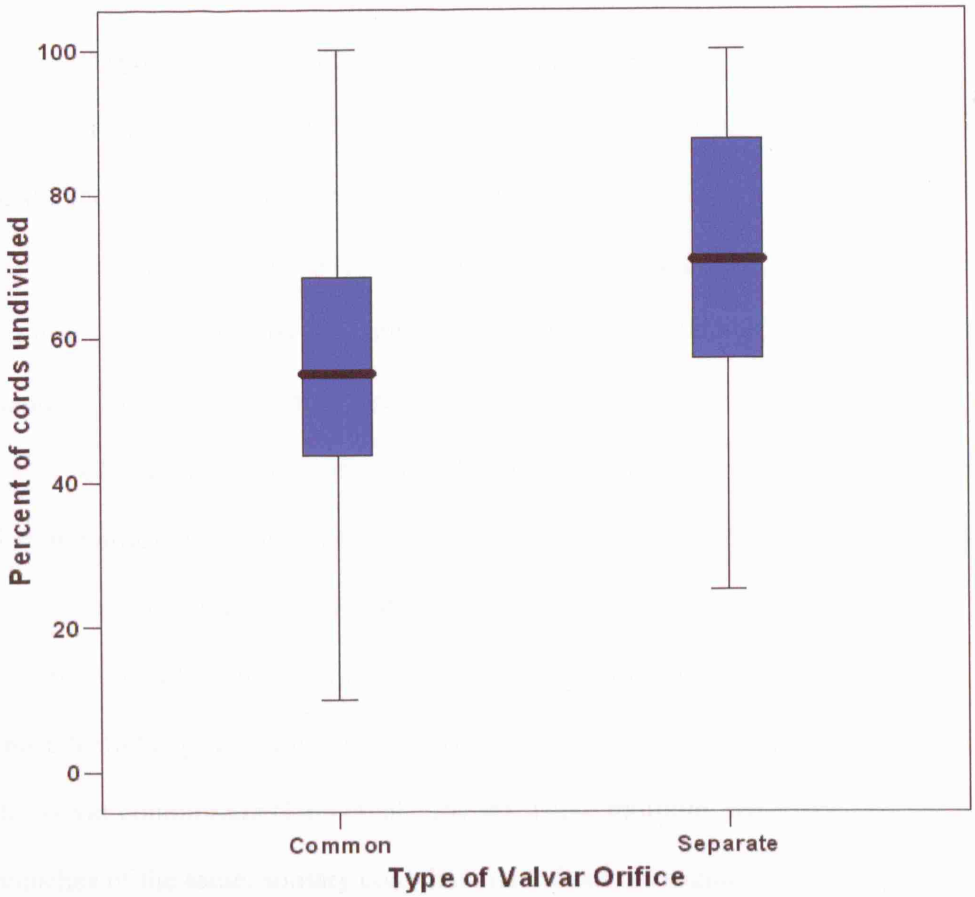

Figure 4.8 Box and Whisker plot showing the difference in the proportion of undivided cords (as defined in Chapter 3) in the defect with the separate and common orifices. In the defect with the common orifice, there was a median of 55.5% (range 10-100%) undivided cords. In the defect with separate orifices, a median of 71.0% cords were undivided (range 25-100%), p = 0.04. This was indicative of greater cordal dysplasia in cases of the defect with separate orifice

Discussion

Surgical management of the zone of apposition between the bridging leaflets in atrioventricular septal defect with common atrioventricular junction is acknowledged to be the most controversial aspect of repair (Hanley et. al., 1993). This region of the tri-leaflet valve is simultaneously the most incompetent component of the native valve, and the prime suspect in early and late post-operative regurgitation (Backer et. al., 1995; Bando et. al., 1995; Castaneda et. al., 1985).

Closer examination of its morphology reveals greater architectural variability than previously thought. What is evident, however, is that it cannot be considered simply to be either a cleft, as in the isolated cleft on the mitral valve, nor a true commissure in the mitral context. In the normal heart, specialized cords run along the entire leaflet edge at the junctions of the aortic and mural leaflet, colloquially known as the valvar commissure (Lam et. al., 1970a). These multiple, fan-shaped cords, are branches of the same, solitary cord that arises from the segment of the papillary muscle immediately beneath its respective leaflet. Thus, a single cord, through multiple divisions is able to support the entire length of the commissure, making for a very simple yet efficient support mechanism.

As we have demonstrated, the zone of apposition in the left atrioventricular valve falls short of this design principle. Given the paucity of cordal support observed, the zone of apposition may be considered to be, at best, an unsupported commissure, doomed to incompetence by this morphologic shortcoming. Even when the cordal support to the edge is extensive, as was observed in cases of defects with a common orifice and Type A arrangement of the superior bridging leaflet, the tendinous cords were not branches of the same cord, but disparate elements arising from the septal crest in a disorganized and haphazard fashion (Figure 4.3). How can these abnormally

shaped, divided and dysplastic cords, numerous as they are, be expected to function in the coordinated manner that the physiology of the normal commissure demands? In the Rastelli C variant, the cordal supply to this coapting zone was almost completely absent. When present, it was confined to the most proximal part of the zone, beneath the kissing points of the valves.

At the most severe end of this morphologic scale were those hearts with separate valvar orifices. In these instances, the zone was often totally unsupported (Figures 4.1c & 4.6). Absence of free-edge cords extended to the ventricular surface of the leaflet that either had no discernable cords, or abnormal cordal forms that gave the leaflet a ribbed appearance. This deficiency at the subvalvar level was quantified in the significantly lower extent of cordal division in hearts with separate valvar orifices.

The coapting surfaces

The variability in the arrangement of the zone of apposition extended to the coapting surface. In the normal mitral valve, the distal ends of both of the leaflets are folded to form a distinctive coapting surface. This free edge is the thinnest and most pliable part of the leaflet, and enables the leaflets to "lock-in" during periods of maximal loading at the peak of ventricular systole. It also gives the closed valvar leaflets the appearance of an unfurled parachute canopy, with the folded edges capturing the regurgitant jet beneath. This arrangement was also seen in atrioventricular septal defects with a common orifice, being best exemplified by the Rastelli Type C arrangement (Figure 4.2). Although the edge of the leaflets at the zone of apposition had very limited cordal support in this arrangement, any effects on overall valvar competence were somewhat ameliorated by the potential for canopy formation by the bridging leaflets, as in the mitral valve. Conceivably, the kissing point of the valve with

a Rastelli C arrangement is its most secure part because of its additional cordal support from the medial papillary muscle of the right ventricle. Furthermore, its irregular surface may permit the opposing leaflets to lock into one another for additional security. The greatest cordal support was, not surprisingly, seen with the Rastelli Type A arrangement. Here, there was not only additional cordal support from the septum to the free edge of the zone of apposition, but the potential for leaflet canopy formation (Figure 4.4). Unlike the mitral, however, fused cords were sometimes found to form part of the coapting surface directly over the crest of the ventricular septum. The greater the degree of cordal fusion, the more difficult it became to identify the anatomic junction between leaflet and underlying cord, especially in the setting of separate valvar orifices where extensive fusion was the norm.

By contrast, leaflet canopy formation was not found to be a feature of the defect with separate orifices. The coapting edge was noticeably thickened, like two plates coming together. There were no discernible kissing points where leaflets could lock together, all in the face of reduced cords and abnormal cordal forms.

The contribution of the inferior bridging leaflet

The inconsistency between the degree of bridging between the superior and inferior bridging leaflets is well recognised (Akiba et. al., 1993; Penkoske et. al., 1985). In this series, there was always some cordal support to the inferior bridging leaflet from the ventricular septum. This was augmented by cords from the inferior papillary muscle, resulting in a plentiful supply to the inferior bridging side of the zone of apposition (Figure 4.5). However, counterpoint to the superior bridging leaflet, where cordal support and canopy formation are the main determinates of competence; leaflet size is an additional determinant at the inferior bridging leaflet side of the zone of apposition.

Thus, the smaller the inferior bridging leaflet, the greater the risk of post-operative regurgitation, presumably because of tissue deficiency at the zone of apposition (Ebels et. al., 1990; Meijboom et. al., 1986) (Figure 4.9). Furthermore, extensive septal tethering of the inferior bridging leaflet, seen among defects with separate orifices not only reduces the effective coapting surface between the leaflets (Ebels et. al., 2002), but angulates the zone of apposition away from its usual perpendicular attitude with respect to the ventricular septum

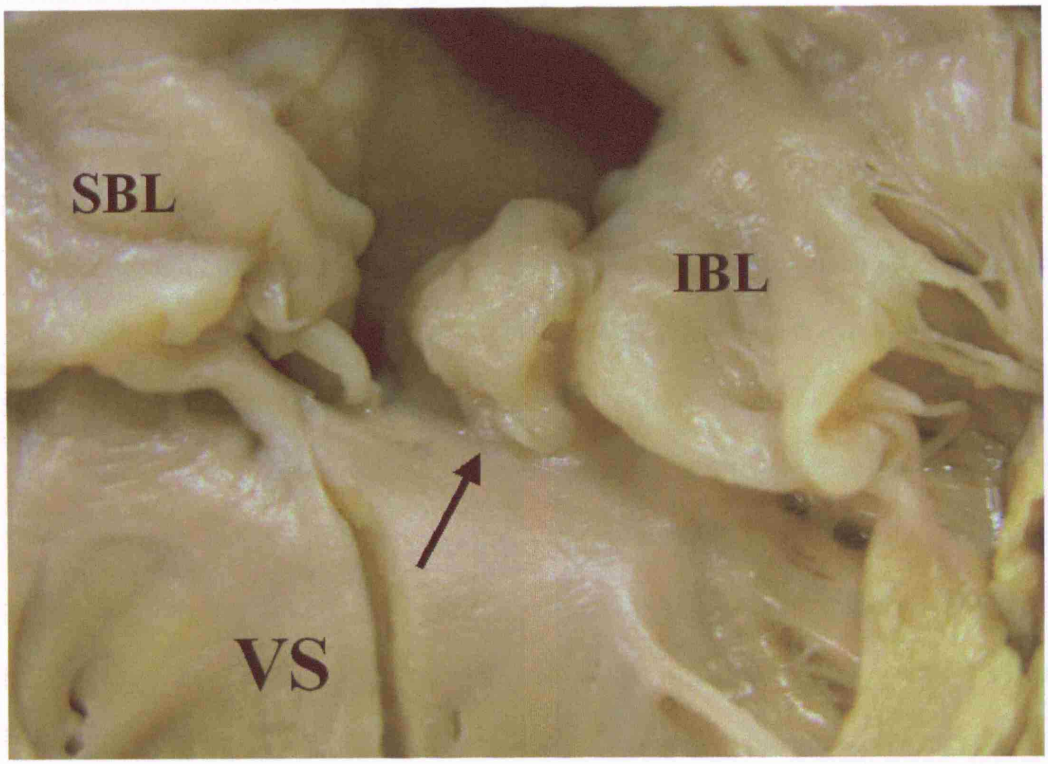

Figure 4.9 Photograph looking at the left ventricular side of the ventricular septum at the Zone of Apposition between the left sides of the superior and inferior bridging leaflets (SBL & IBL, respectively). The black arrow shows that the IBL component of the Zone of Apposition is tethered directly to the crest of the ventricular septum and deficient. This tissue deficiency at this side of the Zone of Apposition may be its source of valvar incompetence.

What is the functional implication of these differences?

All of this suggests that the morphology of the zone of apposition, and hence the adequacy of the competence mechanism, is heterogeneous, depending on the number of valvar orifices, and the permutation of the bridging leaflets. In essence, the morphology lies within a continuum of deformity at both the valvar and subvalvar levels. At the higher end of the scale is the defect with a common orifice, which has some cordal supply to the zone of apposition, albeit a disorganized one, together with leaflet canopy formation, reminiscent of its normal counterpart. At the other end is the defect with separate orifices that not only suffers virtual cordal absence, but leaflets that do not coapt in the most secure manner possible. Such deficiency was observed even in the smallest hearts, so may not necessarily be the result of long-term dysplastic degeneration in hearts with separate orifices that are traditionally operated on at a later age. The principle implication is that although patients may be less symptomatic with an atrioventricular septal defect with separate orifices, their valvar abnormality may be paradoxically worse. Is this bourne out by the clinical experience of valvar regurgitation in this setting? This is difficult to say given the multiplicity of confounding variables inherent in drawing comparisons between different populations. Certainly, subvalvar abnormalities are seen more frequently in hearts with separate orifices (Penkoske et. al., 1985), forming a substrate for left ventricular outflow tract obstruction beyond the narrowing caused by fusing the leaflet to the ventricular septal crest (Ebels et. al., 1984; Gurbuz et. al., 1999). Also, taking all other factors into account, severe preoperative left atrioventricular valvar insufficiency has been seen with a significantly higher frequency in defects with separate orifices (Michielon et. al., 1995), but it is acknowledged that this difference may just reflect selection bias.

Arguments concerning the timing of repair with separate orifices still rage 50 years after the initial successful repair. Whether the weight of this morphologic evidence throws into doubt the present timing and strategy of repair for defects with separate orifices is another issue altogether, but we believe that at the very least, it adds a morphologic dimension to the unresolved clinical debate.

Conclusions

The zone of apposition between the bridging leaflets in atrioventricular septal defects has been described as either a cleft, or a commissure. We have shown that, at best, it is an unsupported commissure, with little resemblance to the normal equivalent in the mitral valve. Given the long-term potential for valvar incompetence at this poorly developed area, this provides further, morphologic, evidence to the modern surgical practice of closing the zone of apposition during repair, where possible.

Unlike previous contentions, this study demonstrates great variability within the morphology of the zone of apposition, depending on the number of valvar orifices and the degree of bridging of the leaflets. Thus, the defect with separate orifices lies at the more abnormal and deficient end of this morphologic scale, at both the valvar and subvalvar level, which has previously been suspected. Whether this implies a change of strategy for repair of defects with separate orifices requires further, clinical, evaluation in the light of these morphologic findings.

Chapter 5: Late incompetence of the left atrioventricular valve following repair of atrioventricular septal defects: the morphologic perspective

Introduction

In this present era of repair of atrioventricular septal defect with common atrioventricular junction, attention has veered from early mortality as the best measure of operative success, and focused onto the long-term quality of life subsequent to surgical repair. This is commonly measured in terms of exercise ability, and freedom from re-operation for residual lesions. Of these latter problems, the most common and troublesome is progressive regurgitation across the newly created left atrioventricular valve, occurring even if the repair was considered robust initially.

The key to the durability of this trifoliate valve is the zone of apposition between its bridging leaflets. Despite the surgical doctrine that complete closure of this zone is the single, and best, way of ensuring competence, the rate of re-operation has remained disconcertingly stagnant over the last thirty years. Why should this be? The reasons are probably multi-factorial, but to help provide some insights, I have returned to first principles. Thus, in this chapter, I have compared the structure of the surgically created septal leaflet of the left valve in atrioventricular septal defects to its normal counterpart, the aortic leaflet of the mitral valve that has been described in Chapter 4. The findings illustrate why this surgically created leaflet will, from the morphologic perspective, always remain the Achilles' heel of surgical repair, even in the best hands.

Methods

Seventy hearts with atrioventricular septal defect with common atrioventricular junction were studied from the 200 specimens kept in the Cardiac Archive, Great Ormond Street Hospital, London (28 hearts), The Frank E. Sherman, Cora C. Lenox Heart Museum, Children's Hospital of Pittsburgh, PA (Angelini et. al., 1988a), and the Cardiac Registry, Children's Hospital, Boston, MA (14 hearts). The hearts selected

were those that permitted direct comparisons to be made with the normal valves. Of those chosen for further study, 26 had separate valvar orifices, the so-called "ostium primum" variant of the lesion, with the remaining 44 possessing a common valvar orifice.

The morphology of the left ventricular components of the superior and inferior leaflets bridging leaflets were studied in those hearts that had been surgically repaired, as well as hearts from patients not undergoing operative intervention. Specimens that were deemed retrospectively unsuitable for biventricular repair were excluded, such as those with a small left ventricle, and those with a solitary left ventricular papillary muscle. Similarly excluded was any hearts with accessory orifices in the left atrioventricular valve, and those with damaged leaflets or subvalvar apparatus.

The following observations were made:

- The shape of the leaflet, comparing the aortic leaflet of the normal mitral valve to the components forming the septal leaflet of the left atrioventricular valve subsequent to surgical repair of atrioventricular septal defect.
- The arrangement of the tension apparatus at the ventricular surface of the leaflet
- The pattern of division of the tendinous cords as they arise from the papillary muscles.

Statistical Analysis

The degree of cordal division was expressed as the median and range. A Mann-Whiney U test was performed in order to compare the incidence of undivided tendinous cords, and the cords that divide to the third generation as defined in Chapter 3.

Results

Shape of the leaflet

The aortic leaflet of the mitral valve is uniformly triangular in shape (Figure 5.1 – upper panel). The base of this triangle is continuous, via the area of aorto-mitral fibrous continuity, with the left and non-coronary leaflets of the aortic valve, this area being thickened at each end as the right and left fibrous trigones. Despite this broad base, the aortic leaflet guards only about one-third of the overall annular circumference of the left atrioventricular orifice. Tendinous cords merge with the sloped sides of the triangle all the way along to its apex, which lies in the axis of the left ventricular outflow tract. As we have seen in chapter 3, these groups of tendinous cords diverge away from either side of the leaflet to insert into their respective papillary muscles.

The newly created septal leaflet of the repaired left atrioventricular valve in hearts with atrioventricular septal defect forms a coapting surface with its smaller counterpart, the left mural leaflet, with the latter guarding less than one-third of the newly created left atrioventricular annulus. When the left ventricular components of the bridging leaflets have been surgically united, a bipartite leaflet is created that is more rectangular, with a triangular recess in its centre that apposes the mural leaflet (Figure 5.1 – right panel).

Figure 5.1 Schematic representation of the aortic leaflet of the mitral valve (left panel) and neo-anterior leaflet of the left atrioventricular valve in repaired atrioventricular septal defect with common atrioventricular junction (right panel). In the mitral valve, the aortic leaflet is triangular in shape with the base continuous with the aortic valve through the aorto-mitral fibrous continuity. Tendinous cords emerge from the sides to insert into the papillary muscles on either side of the left ventricular outflow tract. The neo-anterior leaflet is relatively larger than the mural leaflet and is rectangular, with a central alcove for the mural leaflet. The base of the rectangle relates to the ventricular septum, forming the artificial component of the annulus. Tendinous cords run in the longitudinal axis of the leaflet to insert into papillary muscles plastered to the parietal wall of the ventricle

The septal leaflet thus forms an anti-parietal component that is a composite of different structures, depending on the mode of surgical septation. Specifically,

Following the two-patch repair, the annulus of the left atrioventricular valve is composed of substance of the leaflets sandwiched between the patches used to close the atrial and ventricular components of the septal defect.

- After the single-patch technique, the annulus is composed of the solitary patch, with the septal leaflet sutured to its surface.
- Following the modified single-patch technique, the leaflet is sandwiched between the crest of the ventricular septum and the septal patch

- In the case of atrioventricular septal defect with separate valvar orifices, the base of the leaflet has the patch used to close the atrial component of the defect above, the bridging leaflets themselves being adherent to the ventricular septal crest.

The arrangement of the tension apparatus

Compared to the mitral valve that we had analysed previously, the cordal arrangement of the septal leaflet created by surgical union of the left ventricular components of the bridging leaflets in heart with atrioventricular septal defects was more variable. Unlike the normal, where cords radiate out from the lateral sides of the triangular leaflet in an orderly manner to their corresponding papillary muscle, in all of the cases of atrioventricular septal defect analysed, the cords ran in the longitudinal axis of the potential components of the septal leaflet (Figure 5.1- right panel & Figure 5.2). The cordal axis, therefore, was perpendicular to the ventricular septum, running to the papillary muscles supported in "fore and aft" fashion by the parietal wall.

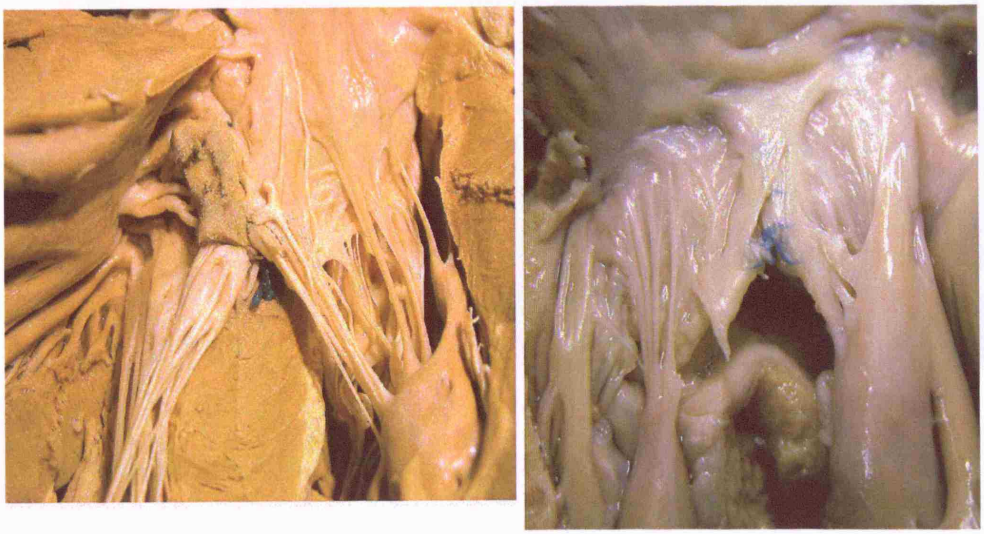

Figure 5.2 Photographs of two examples of the subvalar arrangement of the repaired left atrioventricular valve valve in atrioventricular septal defects. In the left hand panel, the bridging leaflets have been closed with pledgets, and in the right hand panel with unplegeted sutures. There is cordal disorganization in both examples with a greater degree of cordal fusion beneath the right hand example. Compare this to the normal mitral valve, which conforms to a specific design with little morphologic variation.

At the subvalvar level, the cords demonstrated a greater degree of disorganization. In 20 out of the 26 hearts with separate orifices (77%), they were fused, to a variable extent, to the base of the leaflet. This cordal fusion was seen in 30 out of the 44 hearts examined with a common valvar orifice (68%). On other occasions, the leaflet was attached directly to the papillary muscle, with no cords seen on the ventricular aspect of the potential septal leaflet (Figure 5.3).

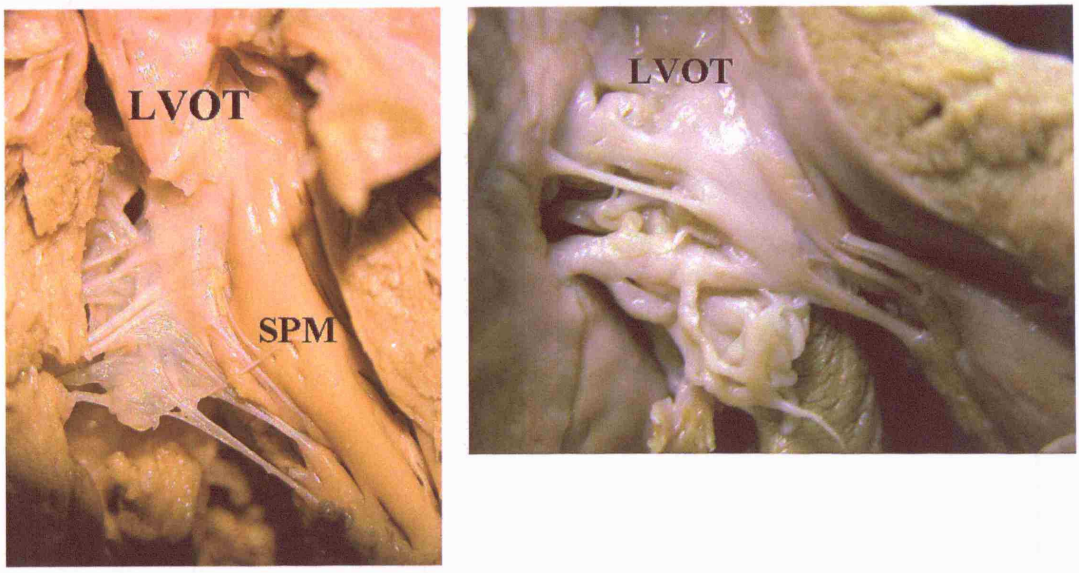

Figure 5.3 Closer views of the subvalvar arrangement beneath the superior bridging leaflet of atrioventricular septal defects with a common valvar orifice, looking from the left ventricular aspect of the superior bridging leaflet. The left hand example shows cordal fusion and organizational disarray. The right hand panel shows abnormal cordal forms and cordal tags, together with central cordal absence. SPM, superior papillary muscle; LVOT, left ventricular outflow tract

As seen in Chapter 4, in atrioventricular septal defects with separate orifices, this cordal fusion and absence was at the more severe end of the scale compared to the defect with a common orifice. In both cases, compared to the mitral valve, undivided cords formed a greater proportion of the total cordal population, with a median of 60.8%, and a range from 10 to 100%, with fewer cords dividing to the third generation, this giving a median 8.7% of the total cords, and a range from 0 to 75% ($p < 0.001$ - Figures 5.4 & 5.5).

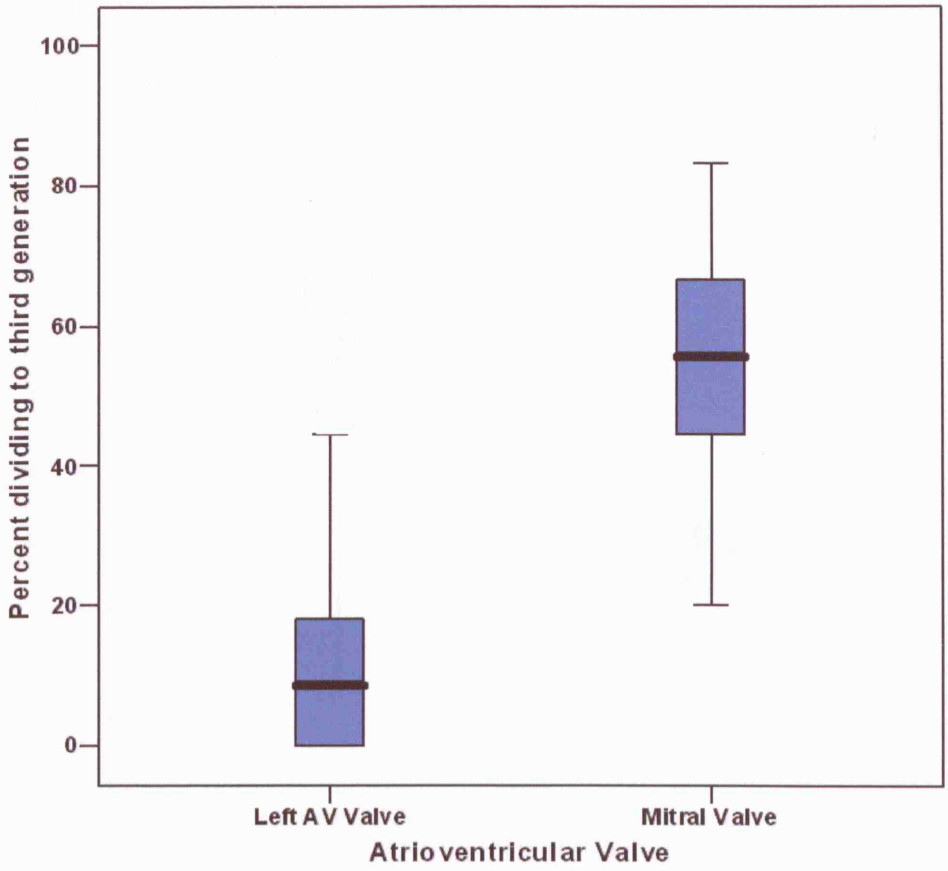

Figure 5.4 Box-plot and Whisker plot of the percentage of tendinous cords that divide to the third generation. In the mitral valve, a median of 54.7% of cords divide to the third generation, compared to the left atrioventricular valve in atrioventricular septal defects where a median of 8.7% of cords divide to the third generation ($p < 0.001$ at 95% CI).

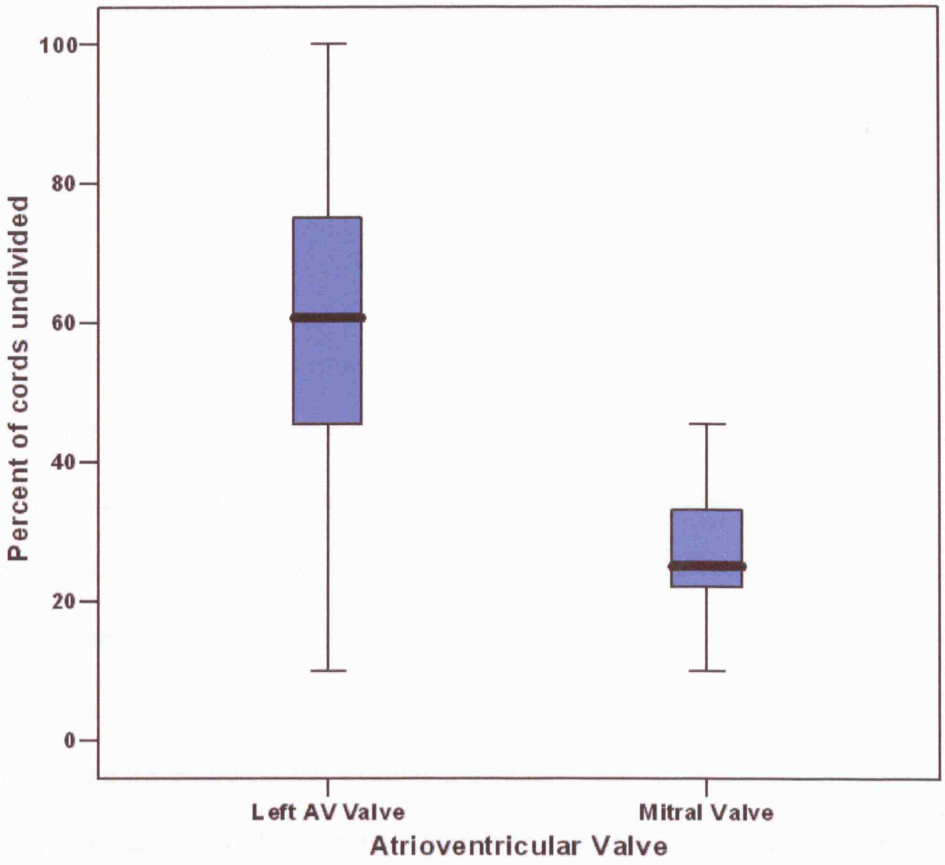

Figure 5.5 Box and Whisker plots demonstrating the percentage of cords found that remain undivided. In the atrioventricular septal defect, a median 60.8% of the cords remain undivided, compared to 26.7% in the mitral valve ($p < 0.001$ at 95% CI)

This greater population of undivided cords gave the septal leaflet a distinctly uni-laminate arrangement compared to the tri-laminate appearance of the aortic leaflet of the mitral valve.

Discussion

As we have previously seen in Chapter 3, the mitral valvar complex is perfectly designed for the task of maintaining atrioventricular competence across all physiologic loading conditions. The annulus forms a D-shaped flexible ring that contracts during systole, permitting the two leaflets to coapt firmly along a solitary zone of apposition (Ho, 2002; Kanani et. al., 2003). The leaflets themselves are folded at their free-edges to form a coapting surface that interlocks with its counterpart. Crucial to ensuring such coaptation during the entire cardiac cycle is the integrity and arrangement of the subvalvar apparatus, that we have seen to consist of a tri-laminar arrangement produced by the pattern of cordal division. Thus, each of the components of the mitral valvar system work in a coordinated and integrated fashion, permitting the best canopy support for the fixed and limited population of cords.

If the end result of this morphologic arrangement of the normal is coordinated function, then based on these observations, this key property is lost in the case of the newly created septal leaflet of the left valve in atrioventricular septal defects. Not only is the branching pattern less advanced than the normal, but cords insert into the subvalvar apparatus in a more disorganized and uncoordinated manner, with dysplastic and bizarre cords running perpendicular to the long axis of the leaflet. The flexibility provided by the laminate arrangement of the aortic leaflet of the mitral valve is also absent in hearts from patients with atrioventricualr septal defects. Consequently, the newly created septal leaflet forms a more rigid structure, potentially reducing its ability

to adapt to changing physiologic conditions. Fear of rendering the leaflet a rigid structure was one of the reasons why, during the earlier era of repair, surgeons left unclosed the zone of apposition between the left ventricular components of the bridging leaflets. The creation of a ridged-flap valve type of arrangement after surgery may also explain why an initially competent tri-foliate valve can become incompetent following closure of the zone of apposition. Added to this is the artificial nature of much of the annular component, a structure that has been created solely to septate the heart, rather than to provide an addition to the already deficient competence mechanism. Any deficiency of the leaflets may further expedite incompetence, as has been seen in situations where the inferior bridging leaflet is smaller than expected (Meijboom et. al., 1986).

Why does the zone of apposition re-open with time?

At re-operation for left atrioventricular incompetence, the regurgitation is usually seen through the distal end of the zone of apposition, where the bridging leaflets have started to disconnect (Figure 5.6).

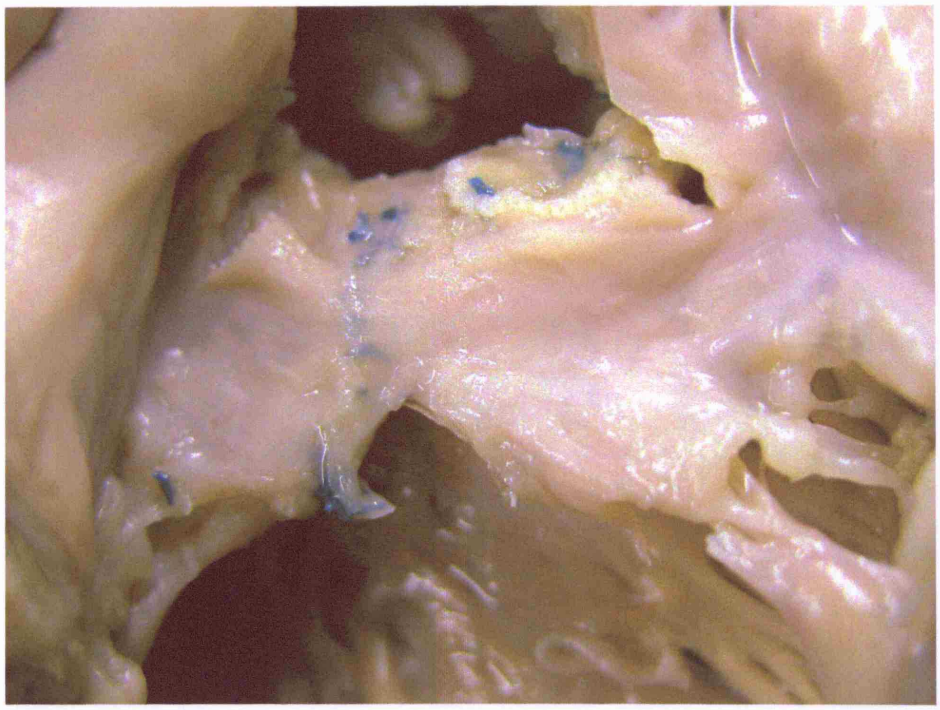

Figure 5.6 Photograph of the surgically-created septal leaflet several years after the repair of a common atrioventricular junction with a common valvar orifice. The superior and inferior bridging components of the valve have separated at the tip of the leaflet, causing regurgitation through the distal end. This may be encouraged by the manner in which the tendinous cords diverge away from the line of closure to insert into their respective papillary muscles

To help understand why this zone has a tendency to re-open, one must consider the nature of this structure, and whether it represents a cleft within the valve, like that of the so-called isolated cleft of the otherwise normal mitral valve, or whether it is a zone of apposition between two of the leaflets of a trifoliate valvar structure (Anderson et. al., 1985). Closer examination reveals that it is neither. As we have seen chapter 3, the ends of the solitary zone of apposition between the two leaflets of the normal mitral valve conform to a very specific pattern, with little variation in the design of the so-called "fan-shaped commissural cord"(Lam et. al., 1970a). In the normal valve, a solitary cord arises from the papillary muscle, and divides into multiple cords that support the entire length of the ends of the zone of apposition. As a result, all of the tension on the ends of

the zone of apposition during ventricular systole is coordinated down a single cord, making the system very efficient (Figure 5.7 – right hand panel and 5.8a).

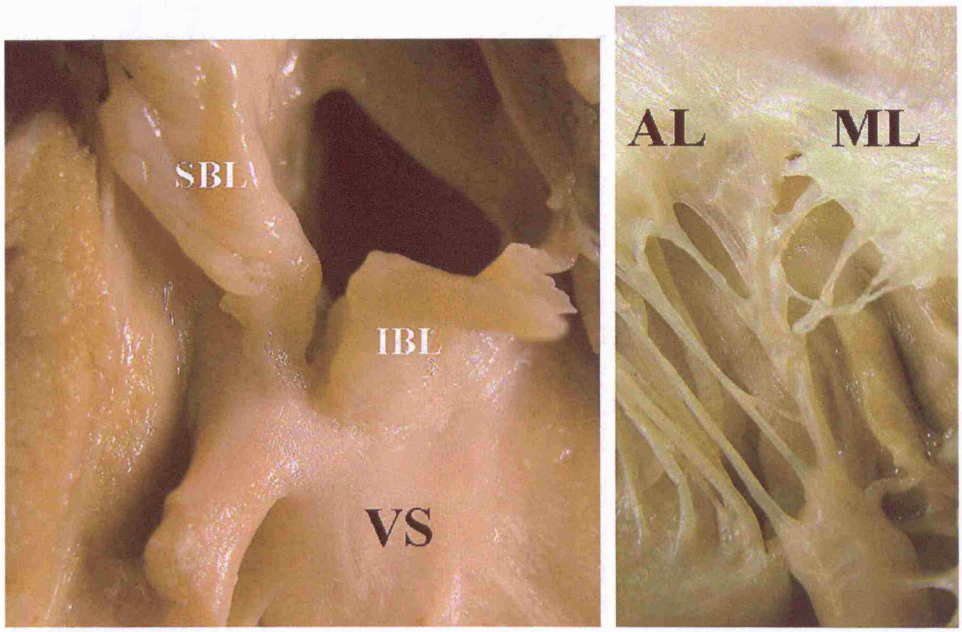

Figure 5.7 The un-repaired zone of apposition in atrioventricular septal defect with separate valvar orifices (left hand panel) compared to the commissure between the aortic and mural leaflet in the normal mitral valve (right hand panel). The zone of apposition forms an unsupported commissure between the bridging leaflets. In this example, taken from a neonatal heart, the bridging leaflets are totally bereft of cordal support. The commissure of the mitral valve is always supported along its entire length by a solitary cord that divides into multiple free-edge cords. SBL, superior bridging leaflet; IBL, inferior bridging leaflet; VS, ventricular septum; AL, aortic leaflet; ML, mural leaflet

In comparison, although the left ventricular components of the bridging leaflets in hearts with atrioventricular septal defect do meet along a zone of apposition, the components of this zone are almost completely unsupported by cords, and lack the design features of the normal "commissure" (Figure 5.7 – left hand panel). Following surgical closure of the zone at operation, cords that diverge from one another to insert into their respective papillary muscles support the tip of the newly created septal leaflet. During loading conditions, the direction of the force, therefore, has a tendency of forcing the leaflets apart (Figure 5.8b).

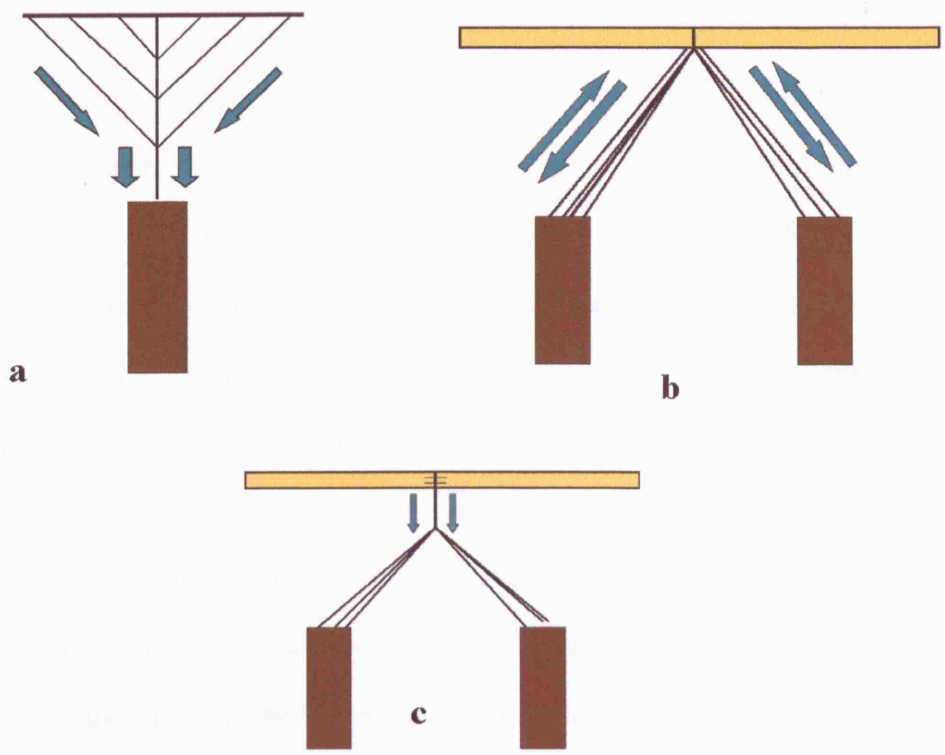

Figure 5.8 A schematic representation of the forces at work on the mitral commissure (a) and the neo-anterior leaflet in atrioventricular septal defects (b). In the mitral commissure, the stress force from the length of the commissure is conceivably directed down the solitary cord, providing the most efficient mechanism. Closure of the zone of apposition in atrioventricular septal defects never attains the normal commissural arrangement since the stress forces on the cords diverge to their respective papillary muscles, producing a tendency for the leaflets to separate. In order to achieve the normal commissural distribution of force, extended zonal closure may have to be undertaken (c). This reduces the stresses on the zone of apposition suture line, but may lead to left atrioventricular valvar stenosis

This is also true of the aortic leaflet of the mitral valve, where the cords diverge at the tip of the triangular leaflet. In the normal state, nonetheless, there is no artificial suture line holding together the whole structure, and acting as a chronic point of weakness. One way to repair the zone in order to distribute the forces like the normal "commissure", taking the stresses off the tip of the leaflet, may be to perform an extended closure where the cords are sutured together at the tip (Figure 5.8c). Alternatively, cords may be transferred from the mural leaflet to the tip of the zone of apposition to restore, in part at least, the normal mechanism of support (Carpentier, 1977; Kuralay et. al., 1999). This may be practically and technically impossible, given the ever-present risk of creating valvar stenosis. It is because this zone is, in effect, an unsupported commissure that surgeons seek, whenever possible, to close fully the zone of apposition. Although the zone may be secure in the short term, its unsupported nature betrays its competence over the longer term. This was understood and demonstrated by Carpentier (Carpentier, 1977), whose system of tri-leaflet repair aimed to restore the normal commissural arrangement through additional surgery to the annular attachments of the leaflets and tension apparatus. Compounding this chronic tendency for separation of the leaflets is progressive dilation of the composite artificial annulus. Consequently, regurgitation begets regurgitation in the face of increased stress on the suture line.

Conclusion

It is evident that, even with adequate closure of the zone of apposition following repair of atrioventricular septal defects, the surgeon can never recreate the normal mitral valve. From the outset, every component of the valvar apparatus is deficient compared to the normal arrangement. The annulus is a composite structure with artificial components, while the restored septal leaflet has altered geometry, with a rotated axis of closure compared to the normal. The subvalvar apparatus is characterized by disorganization, dysplasia, and disarray. Once closed, the forces generated by cords arranged in the longitudinal axis of the leaflet may paradoxically encourage re-opening at the tip of the newly created leaflet, especially if there is already some annular dilation. All of these factors interplay to encourage the long-term failure of the valve despite initial competence. The great morphologic variability seen within this context may explain why some valves are more robust than others. Irrespective of the quality of repair, given the deficiencies so described, the left atrioventricular valve is designed to fail from the outset

Chapter 6: Repair of atrioventricular septal defects at Great Ormond Street Hospital 1994-2004

Patients and Methods

Between January 1994 and December 2004, 313 patients underwent repair of atrioventricular septal defect with common atrioventricular junction at Great Ormond Street Hospital for Children, London. Of these, 202 (64.5%) patients had a common valvar orifice, and 110 (35.1%) had separate orifices. Patients with the so-called transitional defect were included among those with a common orifice. Only those patients having bi-ventricular repair were included in the study. One hundred and eighty one patients (57.8%) had trisomy 21. Of these patients, 145 had a common orifice (80.1%) and 36 (19.9%) had separate orifices. Other genetic anomalies exhibited were Noonan's syndrome in 2 patients; 8p deletion in 1 patient; 4q deletion in 1 patient and Kleinfelter's syndrome in 1 patient .

Age and weight at repair

With common orifice

The median age at repair for defects with a common orifice was 4.8 months (range 18 days to 4.6 years), and the median weight 4.7 kg (range 2.1-40 kg)

With separate orifices

For defects with separate orifices, the median age at repair was 42.8 months (range 2.1 – 13 years), and median weight 11.3 kg (range 2.5-71.6 kg).

Associated Cardiac Defects

With common orifice

Sixty-five patients (32.1%) with common orifice also had a patent arterial duct. Ninety-two (45.5%) had a defect in the oval fossa identified at operation. Other minor anomalies identified were, left superior caval vein in 12 (5.9%), right aortic arch in 1. Major defects identified were, tetralogy of Fallot in 14 (6.9%) and isolated pulmonary stenosis in 5 (2.4%), coarctation in 5 (2.4%), and additional mid-muscular ventricular septal defect in 1. Of the 202 patients with a common orifice that underwent bi-ventricular repair, 16 patients (7.9%) had ventricular imbalance due to a small left ventricle in 12, and a small right ventricle in 4.

Major left atrioventricular valvar abnormalities were dual orifice in 9 (4.4%), solitary papillary muscle arrangement in 3 (1.5%), and valvar dysplasia/leaflet deficiency identified at operation in 14 (6.9%). In 7 (3.4%) patients, there was no atrial component identified at operation.

With Separate orifices

Ten patients (9%) with separate valvar orifices had a patent arterial duct, and 35 (31.8%) demonstrated a defect in the oval fossa at operation. Eight patients (7.2%) had a co-existing left superior caval vein. Other major anomalies identified were; partitioned left atrium in 2 (1.8%); pulmonary valvar stenosis in 3 (2.7%); Ventricular imbalance in 4 (3.6%), all due to a small left ventricle. Abnormalities of the left atrioventricular valve identified were; dual orifice in 3 (2.7%); and severe valvar dysplasia in 10 (9%). In 12 patients (10.9%), there was pre-operative shunting through the zone of apposition giving the echocardiographic appearance of a ventricular component to the defect.

Previous Surgical procedures

Eleven patients had undergone previous palliative pulmonary trunk banding, all having a defect with a common orifice. In 3 of these, it was in association with repair of coarctation of the aorta and ligation of the arterial duct. Since the year 2000, only 3 patients had initial palliative banding, all in the presence of pre-operative sepsis and multi-organ failure.

Six patients out of the 14 with teratology of Fallot (42.8%) had had a previous systemic to pulmonary shunt prior to definitive repair, 1 with bilateral modified Blalock-Taussig shunt, and 5 with unilateral Blalock-Taussig shunt.

One patient, with separate orifices, had undergone previous repair of an aorto-pulmonary window, and another, with a small left ventricle and common orifice, had undergone previous stage 1 Norwood procedure. Thus 183 patients with a common orifice (90.6%), and 110 patients with separate orifices (100%) had undergone primary repair of atrioventricular septal defect.

Operative technique

Repair was carried out using cardiopulmonary bypass. For defects with common orifice, excluding those with small ventricular component or tetralogy of Fallot, the mean bypass time was 117.4 minutes (64-346 minutes) and cross clamp time 71.6 (30-122 minutes). In the presence of tetralogy of Fallot, the mean bypass time was 139.5 minutes (104-182mins) and cross clamp time 88.9 minutes (76-106 minutes). For defects with a separate orifice, the mean bypass time was 88.5 minutes (41-169 minutes) and mean cross clamp time 53.0 minutes (19-102 minutes).

For defects with a common orifice, all cases bar 14 were repaired with a double patch technique. In 11 cases, repair was undertaken with a single patch technique due to absence of the atrial component. Three cases were repaired with the modified single patch technique with suturing of the bridging leaflets to the septal crest to close the ventricular component. In one of these, the modified single patch repair was converted to a double patch repair after it was found that there was left ventricular outflow tract obstruction.

For defects with tetralogy of Fallot, 8 out of 14 were repaired with patch augmentation of the right ventricular outflow tract, and 1 with a right ventricle to pulmonary trunk conduit.

In all cases, where possible, the zone of apposition between the bridging leaflets was closed with bicuspidization of the left atrioventricular valve. However, for defects with a common orifice, in 3 (1.48%) cases, this was not possible. In one case, there was a small left ventricle with solitary arrangement of the papillary muscle and risk of subsequent left atrioventricular valvar stenosis. In another, the patient had a small body surface area with a dysplastic and friable-

looking valve. In another there was an incomplete tongue of valvar tissue between the bridging leaflets producing two competent zones of apposition.

In the setting of defects with separate orifices the zone of apposition was left unclosed in 6 (5.45%) cases due to a small left ventricle and absence of the mural leaflet in the setting of a solitary papillary muscle arrangement.

Annuloplasty of the left atrioventricular valve was performed in 7 cases (3.46%) with common orifice and 5 (4.54%) of defects with separate orifices. Commissuroplasty was performed in 10 (4.95%) cases of common orifice and 3 (2.72%) cases of separate orifices.

Mortality

With common orifice

The overall 30-day mortality between 1994-2004 in the setting of a common orifice was 11/202 = 5.4%. Since the year 2000, the 30-day and in-hospital mortality was 0%

Among the 188 patients with common orifice without tetralogy of Fallot, 9 (4.8%) patients died within 30 days of the operation. In the setting of tetralogy of Fallot, the 30-day mortality was 14.3% (2 out of 14 patients).

With separate orifices

Between 1994 - 2004, no patients died within 30 post-operative days. The in- hospital mortality was 1 (0.9%), occurring on post-op day 182. The patient was intubated before the operation, having previously been palliated with a pulmonary trunk band for sepsis in the context of severe dysplasia and incompetence of the left atrioventricular valve. Post-operatively, the incompetence persisted requiring replacement of the valve with a mechanical prosthesis. Sepsis and bowel necrosis supervened.

Table 6.1 (next page) Demographics of in-hospital mortalities for repair of atrioventricular septal defects at Great Ormond Street Hospital from 1994-2004.

Case No	*Year of Op*	*Age/months*	*Karyotype*	*Time of Death post op/days*	*AVSD type*	*Associated Defects*	*Cause of Death*
1	1994	9	Trisomy 21	19	Common	PDA, ASD	Tension pneumothorax
2	1994	4	Trisomy 21	On Table	Common	ASD, LAVV dysplasia	LOS and intractable LAVVR
3	1995	1	Normal	On Table	Common	PDA, ASD, small LV, previous CoAc repair	LOS
4	1995	2	Trisomy 21	20	Common	ASD intubated pre-operatively	Sepsis, pulmonary hypertensive crises
5	1996	382	Trisomy 21	3	Common	Tetralogy of Fallot	LOS and renal failure
6	1996	1	Trisomy 21	On table	Common	No Notes available	No Notes available
7	1997	10	Trisomy 21	18	Common	ASD, small muscular VSD	PHT crisis, ARDS, pneumococcal sepsis
8	1998	1	Normal	2	Common	PA, ASD, dysplastic LAVV, simultaneous Coarctation repair	Intracerebral bleed, severe LAVVR and staphylococcal sepsis
9	1998	1	Trisomy 21	15	Common	ASD, PDA, DOUBLE ORIFICE LAVV	Severe LAVVR, LOS, klebsiella sepsis
10	1999	9	Trisomy 21	13	Common	PDA, ASD	Unexplained cardiac arrest
11	1999	7	Normal	1	Common	Tetralogy of Fallot, previous aorto-pulmonary window repair	Unexplained cardiac arrest
12	2004	5	4q31 deletion	182	Separate	Severe valvar dysplasia and incompetence	Required LAVV replacement, LOS, sepsis supervened and necrotic bowel

Risk factors for early mortality

Table 6.2 outlines the statistical significance of various potential risk factors identified for early mortality of the defect with a common orifice. The only factors identified by univariate (χ^2) analysis were pre-operative intubation ($p = 0.004$), dysplasia of the left atrioventricular valve ($p = 0.002$), the era of operation from 1994-2000 ($p = 0.002$), and age less than 45 days old ($p < 0.01$).

Table 6.2 Summary of the potential risk factors associated with early mortality following repair of atrioventricular septal defects. Statistical analysis performed by univariate analysis **(see next page)**

Variable	*Mortality with Variable*	*Mortality without Variable*	*p Value*
Era of operation 1994-2000	11/118 = 9.3%	0/84 = 0%	0.002
Pulmonary hypertension	2/16 = 12.5%	9/186 = 4.8%	0.214
Pre-operative intubation	3/7 = 42.9%	8/195 = 4.1%	0.004
Trisomy 21	7/145 = 4.8%	4/49 = 2.9%	0.626
Tetralogy of Fallot	2/14 = 14.3%	9/188 = 4.8%	0.173
Double orifice LAVV	1/9 = 11.1%	10/193 = 5.2%	0.404
Dysplastic LAVV	4/16 = 25%	7/185 = 3.8%	0.008
Parachute LAVV	0/8 = 0%	11/193 = 5.7%	0.06
Small left ventricle	1/17 = 5.9%	10/185 = 5.4%	0.631
Small right ventricle	0/3 = 0%	11/199 = 5.5%	0.844
Pre-operative moderate or severe LAVV regurgitation	3/26 = 11.5%	8/176 = 4.5%	0.156
Previous pulmonary trunk banding	1/10 = 10%	10/192 = 5.2%	0.438
Pre-operative weight less than 4kg	2/35 = 5.7%	2/103 = 1.9%	0.285
Pre-operative age greater than 7 months (excluding ToF)	3/64 = 4.7%	9/187 = 4.8%	0.630
Pre-operative age less than 45 days old	4/10 = 40%	5/178 = 2.8%	<0.001

Re-operation for Left atrioventricualr valvar regurgitation

Thirty-two patients underwent re-operation for post-operative regurgitation of the left atrioventricular valve. Nineteen were patients with common orifice (9.4% of those with common orifice), and thirteen had separate valvar orifices (11.8% of those with separate orifices). All patients had undergone repair of the left atrioventricular valve at the original operation. In 17 patients, the leak through the valve was at the distal end of the zone of apposition. Other causes were central regurgitation, regurgitation through the commissure between the bridging leaflets and the mural leaflet, and incompetence due to tearing of the leaflets at the suture line. Four patients, three with common orifice and one with separate orifices, had a further re-repair, with one of these having a second re-operation resulting in valvar replacement. This is summarized in Table 6.3

Table 6.3 Cases of re-repair of the left atrioventricular valve for both defects with common and separate orifices. (see next 3 pages)

Valvar orifices	*Other diagnosis*	*Trisomy 21?*	*Year of Operation*	*Time to re-operation*	*Morphology of regurgitation*	*Further re-operations?*
Common	Accessory orifice left AV valve, solitary papillary muscle, small LV	No	2004	15 days	Tear in the bridging leaflets at the ZoA	No
Common	Unusual cleft of the IBL	Yes	2002	10 days	Small tear in SBL and leak through IBL cleft	No
Common	None	Yes	2001	13 days	Not available	Left AV valve replaced 2 months after original operation
Common	Pre-op pulmonary hypertension	Yes	1998	17 days	Leak through distal end of the ZoA	No
Common	Accessory orifice left AV valve, valvar dysplasia	Yes	1998	1 day	Through perforated SBL	No
Common	Dysplastic Left AV valve	Yes	1997	24 months	Leak through distal end of the ZoA	No
Common	None	No	1998	10.6 months	Not available	No
Common	Pre-op pulmonary hypertension	Yes	1997	17 days	Tear in the SBL	No
Common	Accessory orifice left AV valve, small LV	No	1997	10 days	Tear in the SBL	No

Valvar orifices	*Other diagnosis*	*Trisomy 21?*	*Year of Operation*	*Time to re-operation*	*Morphology of regurgitation*	*Further re-operations?*
Common	Severe pre-op left AV valve regurgitation small LV	Yes	1997	3 days	Tear in the SBL	Yes, left AV valve replaced at 13 months
Common	None	Yes	1996	4 days	Not available	No
Common	Left AV valve dysplasia with severe regurgitation	No	1996	4 days	Central regurgitation	Re-repair 1 month post-op, then replaced 1 month later
Common	Severe pre-op regurgitation, cleft in IBL	No	1996	6 days	Leak through IBL cleft	No
Common	Small left ventricle	No	1996	53 months	Leak through distal end of the ZoA	No
Common	None	Yes	1995	60 months	Leak through distal end of the ZoA and centrally	No
Common	None	No	1995	75 months	Through distal ZoA and SBL perforation	No
Common	Dysplastic left AV valve with severe pre-op regurgitation	Yes	1995	81 months	Central regurgitation	No
Common	Accessory orifice left AV valve, severe regurgitation	No	1994	3 days	Tear in the IBL	No

Valvar orifices	*Other diagnosis*	*Trisomy 21?*	*Year of Operation*	*Time to re-operation*	*Morphology of regurgitation*	*Further re-operations?*
Common	None	No	1994	55.4 months	Through distal ZoA	No
Separate	Severe pre-op regurgitation	No	2004	79 days	Through distal ZoA	No
Separate	Dysplastic left AV valve	No	2003	53 days	Central regurgitation	Valve replaced 3 months post-op
Separate	None	No	2003	51 days	Leak through ZoA	No
Separate	None	No	2001	112 days	Between SBL and ML	No
Separate	None	No	2001	20.5 months	Leak through distal end of the ZoA and centrally	No
Separate	None	No	2001	35 days	Through distal ZoA	No
Separate	Dysplastic left AV valve with severe pre-op regurgitation	No	1997	5 days	Torn SBL	No
Separate	Dysplastic left AV valve	No	1997	3 days	Through distal ZoA	No
Separate	None	Yes	1996	24.7 months	Through distal ZoA	No
Separate	Severe pre-op regurgitation	No	1996	23.8 months	Through distal ZoA	No
Separate	None	No	1995	76.3 months	Through distal ZoA	No
Separate	None	No	1995	59.5 months	Through distal ZoA	No

Valvar orifices	*Other diagnosis*	*Trisomy 21?*	*Year of Operation*	*Time to re-operation*	*Morphology of regurgitation*	*Further re-operations?*
Separate	None	Yes	1994	90 months	Through distal ZoA	No

Risk factors for re-operation

The median follow-up time after the first operation was 37.5 months (range 0 – 132.6 months).

With Common orifice

Follow-up of patients were analysed with a Kaplan-Meier survival analysis in order to determine the clinical variables that posed a significant risk for re-operation on the left atrioventricular valve (Figures 6.1 to 6.3).

Re-operation on the left atrioventricular valve was associated with the absence of trisomy 21, ($p = 0.008$). Children with valvar dyasplasia were also found to have a higher rate of re-operation ($p = 0.0406$), as were those with an accessory orifice to the left atrioventricular valve ($p = < 0.001$), and a small left ventricle ($p = 0.005$).

The presence of moderate to severe left atrioventricular valver regurgitation was found to be of borderline significance ($p = 0.05$).

The risk for re-operation was not associated with the presence of tetralogy of Fallot ($p = 0.2$), the era of operation before 2000 ($p = 0.1$), being less than 4kg

at the time of operation (p = 0.44), nor being greater than 7 months old at the time of operation (p = 0.47).

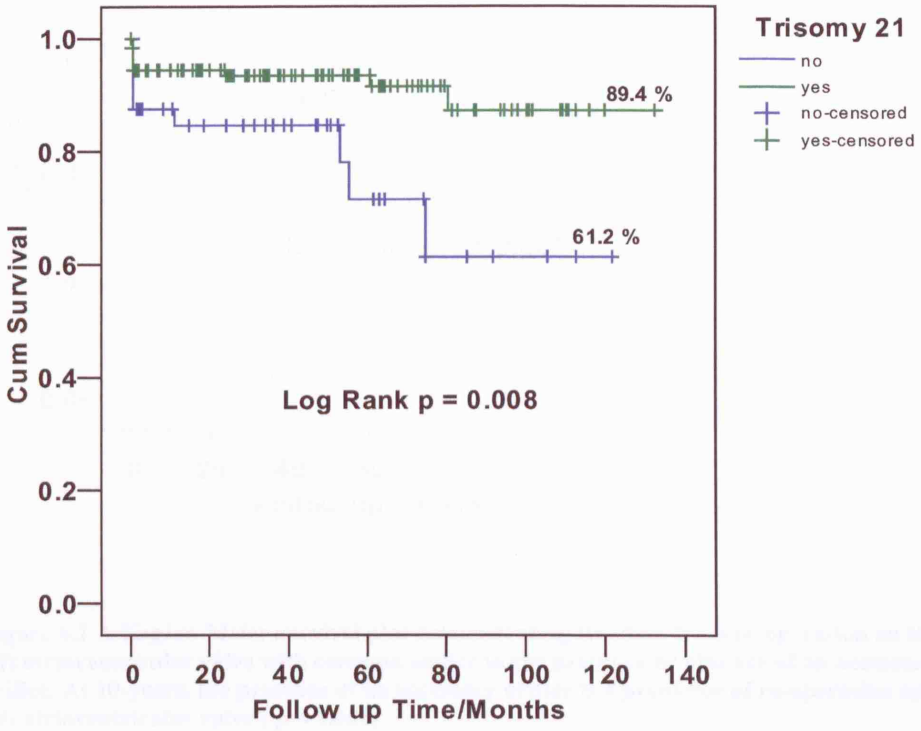

Figure 6.1 Kaplen-Meier Survival plot demonstrating freedom from re-operation on the left atrioventricular valve in a common orifice with the presence or absence of trisomy 21. This shows an 89.4 % freedom from re-operation at 10 years in the presence of trisomy 21 compared to 61.2 % in the absence of trisomy 21 (Log rank p = 0.008)

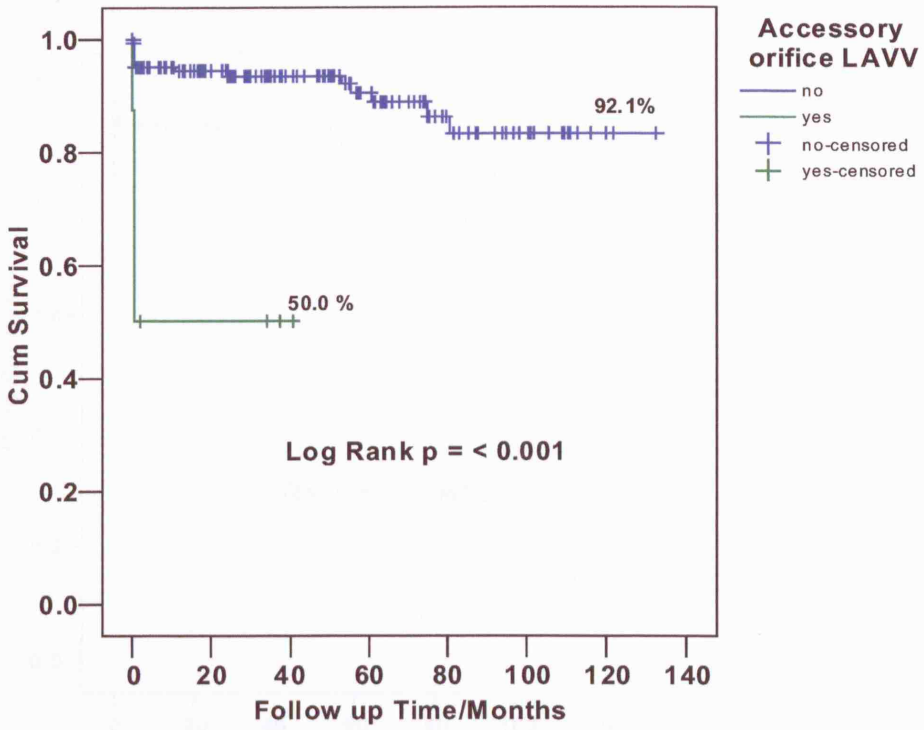

Figure 6.2 A Kaplen-Meier survival plot demonstrating freedom from re-operation on the left atrioventricular valve with common orifice in the presence or absence of an accessory orifice. At 10-years, the presence of an accessory orifice is a predictor of re-operation on the left atrioventricular valve ($p < 0.001$)

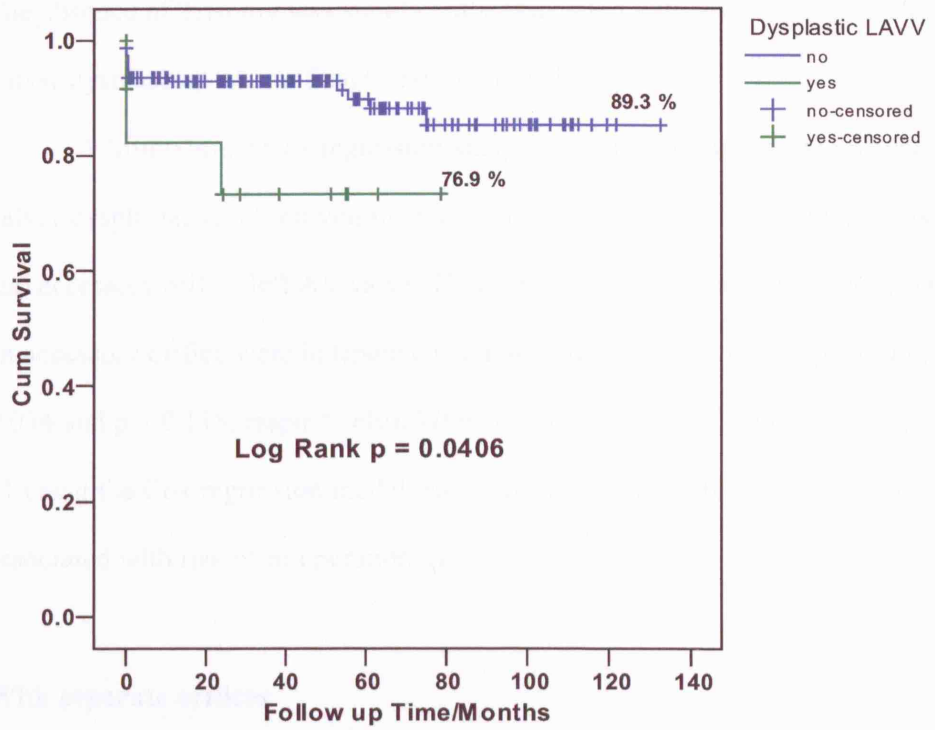

Figure 6.3 A Kaplen-Meier survival curver demonstrating 10-year freedom from re-operation on the left atrioventricular valve in the common orifice defect in the presence and absence of a dysplastic left atrioventricular valve. This was found to be a significant risk factor for long-term re-operation on the valve

The absence of Trisomy was significantly associated with left atrioventricular valvar dysplasia (Fisher's Exact Test, p = 0.004).

A Multivariate Cox regression analysis was performed on the presence of valvar dysplasia, small left ventricle, moderate/severe left AV valve regurgitation and accessory orifice left AV valve. This demonstrated that a valvar dysplasia and an accessory orifice were independently associated with risk of re-operation (p = 0.034 and p = 0.118, respectively). When controlling for the influence of Trisomy 21 using the Cox regression model, valvar dysplasia in itself was independently associated with risk of re-operation, (p = 0.005).

With separate orifices

In the presence of Trisomy 21, the cumulative 10-year freedom from re-operation was 95.6% compared to 65% in children of normal karyotype (Log Rank p = 0.0386) (Figure 6.4). Similarly, in the presence of a dysplastic left atrioventricular valve, the cumulative 10-year freedom from re-operation was 62.5% compared to a non-dysplastic valve with a 95.6% freedom from re-operation Log Rank p = 0.0129 (Figure 6.5). Being over the age of two at operation was found to be associated with a greater 10-year freedom from re-operation, being 94.4% compared to 59.2% freedom in those less than two, Log Rank p = 0.0102 (Figure 6.6). However, if those cases that were re-operated within one year are excluded, then the effect of age on re-operation in rendered insignificant; Cumulative freedom from re-operation at 10-years at age less than 2

is 68.6% compared to 86.5% over 2 years of age, Log Rank p = 0.765 (Figure 6.7). Severity of pre-operative left atrioventricular valvar regurgitation and early era of operation were not associated with an increased risk of re-operation at 10 years, Log Rank p = 0.508 and 0.362, respectively.

If both significant factors, absence of trisomy 21 and pre-operative dysplasia of the left atrioventricular valve are entered into a multivariate model, both factors are found to be independently significant (p = 0.01 and 0.026 respectively).

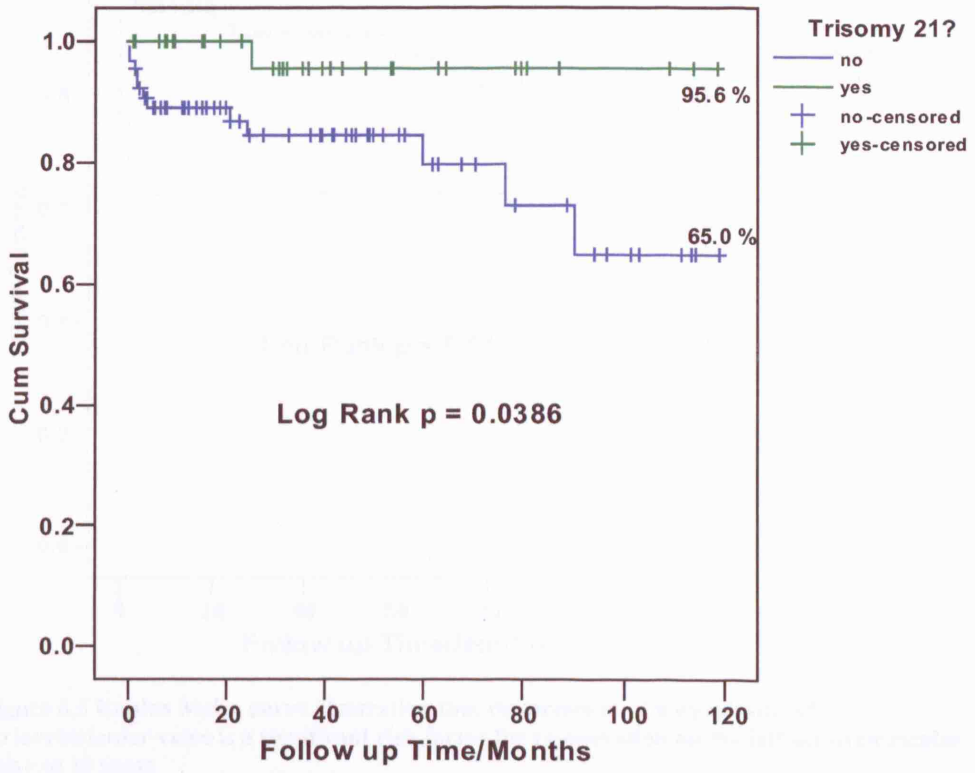

Figure 6.4 A Kaplen Meier survival curve showing the influence of trisomy 21 on the 10-year freedom from re-operation on the left atrioventricular valve in the defect with separate orifices. Absence of trisomy 21 is a significant risk factor for re-operation at 10 years (p = 0.0386)

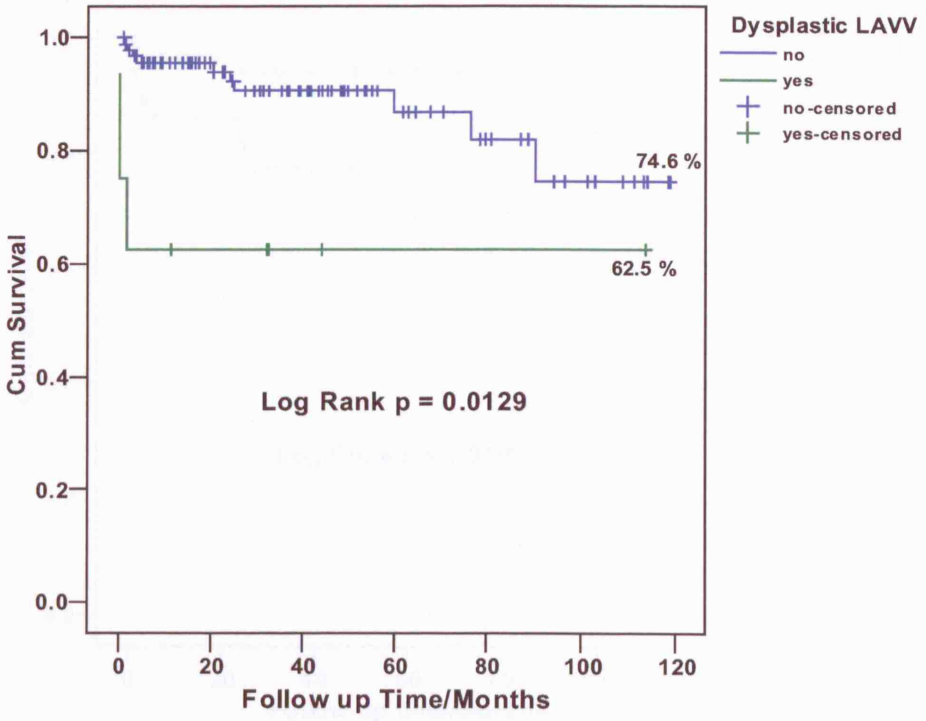

Figure 6.5 Kaplen Meier curve illustrating that the presence of a dysplastic left atrioventricular valve is a significant risk factor for re-operation on the left atrioventricular valve at 10 years

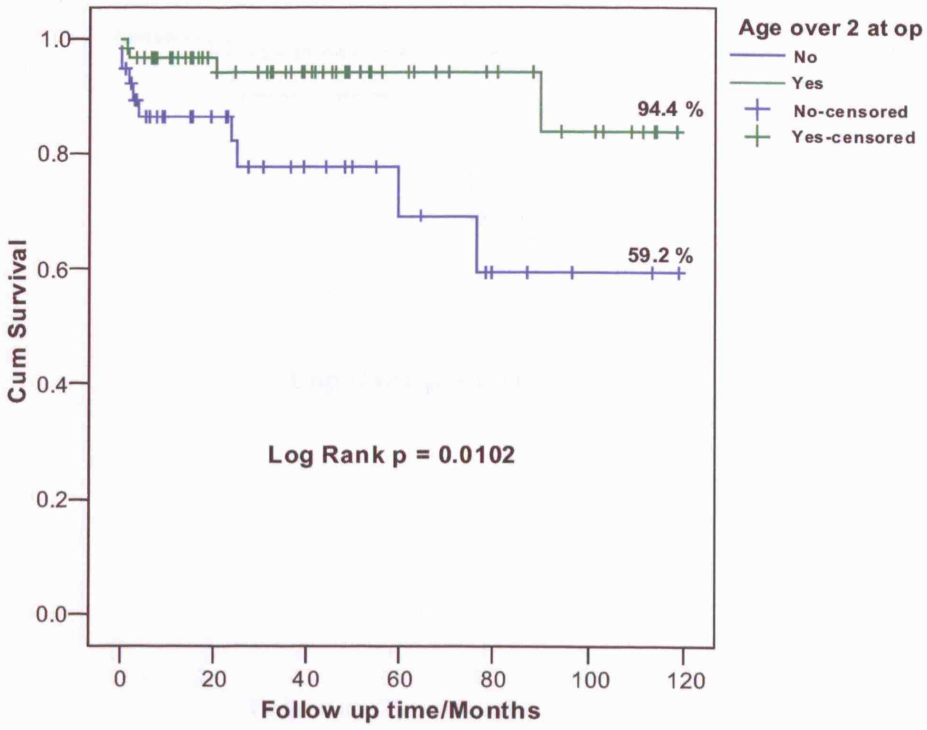

Figure 6.6 Kaplen-Meier survival curve demonstrating that age over the age of 2 is associated with a significantly reduced risk of re-operation at 10-years. This is in contrast to figure 6.7

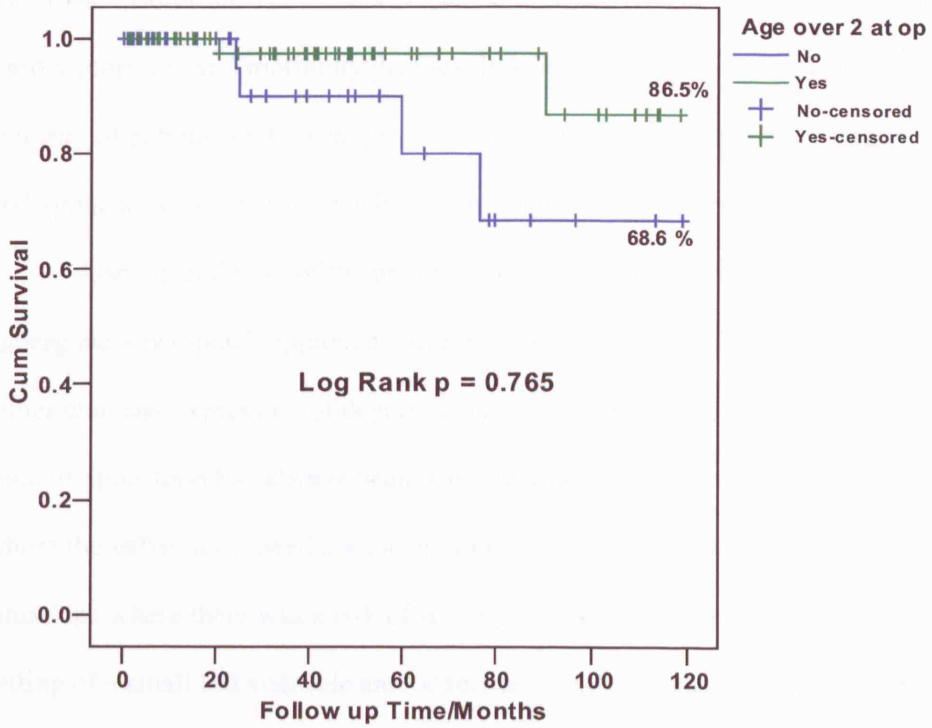

Figure 6.7

Kaplen-Meier curve showing that the significance of age at operation on the 10-year freedom from re-operation is lost if excluding cases that had re-operation within 1 year, thus excluding those who were operated on early for severe dysplasia and regurgitation. After this exclusion, it shows that the protective effect of older age seen in the previous graph is lost

Discussion

This study has analysed retrospectively the results of repair in the modern era in one institution. The results presented here are typical of other units, with similar mortality and morbidity profiles. In keeping with modern practice, the vast majority of patients underwent primary repair, and since 2000 only 3 had undergone a two-staged approach with initial pulmonary trunk banding, for sepsis.

Also, virtually all of the patients with a common orifice defect had undergone a two-patch approach, but this was a reflection of preferential practice rather than any expression of departmental policy. However, routine closure of the zone of apposition has always been departmental practice, even in situations where the valve has looked competent initially. It was only left unclosed in those situations where there was a risk of subsequent valvar stenosis, namely in the setting of a small left ventricle and/or solitary papillary muscle arrangement of the left ventricle. Interestingly, in one case, the pattern of fusion of the bridging leaflets across the ventricular septum had produced two competent zones of apposition. This arrangement has, never been described in the literature, so the surgeon elected to leave the morphology alone in the fear that valvar incompetence could have resulted

Surgical Mortality

There has been a striking reduction in the early and late post-operative mortality since the dawn of repair when mortality ranged from 30 to 60% (Figure 6.8). In the current era, in the situation of a common orifice with no associated defects, balanced ventricles, and the absence of pulmonary hypertension, the mortality in all centres reporting is less than 5.5 %, and usually in the order of 1.5-

3%. The results for the 30-day presented here are in line with these other units, but more specifically, there have been no mortalities for the defect with the common orifice since 2000, and none for the defect with separate orifices since at least 1994. This emphasises the belief that mortality, alone, is not the best contemporary judge of surgical success.

What of the risk factors associated with early mortality? The factors analysed here were those that had previously identified by some groups as being significant. The only factors that were identified statistically as significant in this cohort were; pre-operative intubation, dysplasia of the left atrioventricular valve, the era of operation from 1994-2000, and age less than 45 days old. It is understandable why these may have been identified, especially the era of repair, owing to improved peri-operative management of these patients. Pre-operative intubation (Alexi-Meskishvili et. al., 1997) is an indicator of incurrent illness, such as sepsis, prematurity or severe pulmonary hypertension. Table 6.2 identifies some risk factors that were not identified here, but identified by some other groups, such as tetralogy of Fallot, dual orifice of the left atrioventricular valve and unbalanced ventricles (Table 6.4). One reasonable explanation for the disparity of the findings here with the findings of other groups lies in the small numbers confounding any conclusion drawn from the statistical analyses. This highlights the problem of the modern era; that the numbers of early mortalities are often too small to derive robust conclusions. All we can say is that, for a number of reasons, patients are being kept alive for longer.

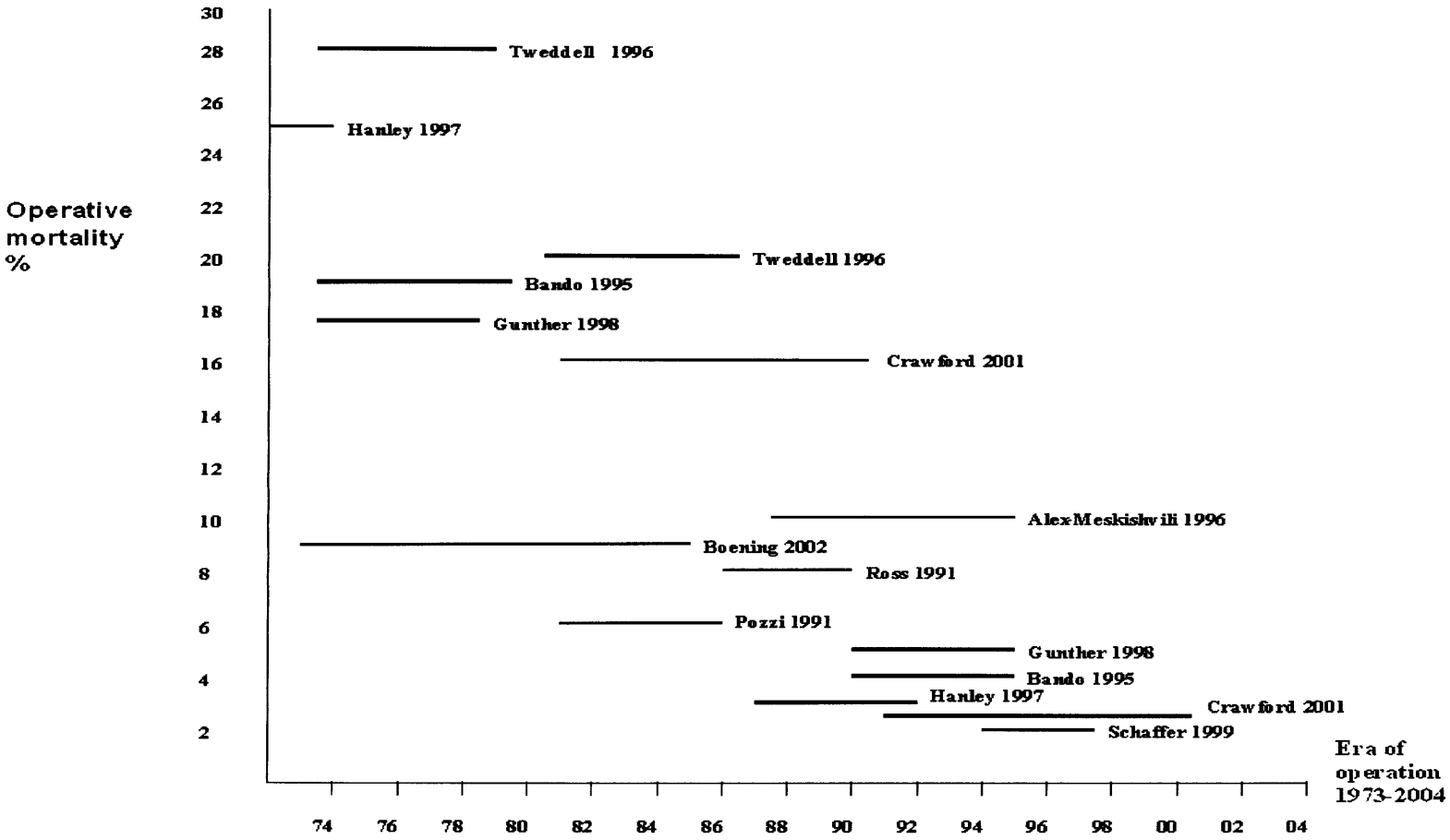
Operative mortality %
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
Tweddell 1996
Hanley 1997
Tweddell 1996
Bando 1995
Gunther 1998
Crawford 2001
AlexMeskishvili 1996
Boening 2002
Ross 1991
Pozzi 1991
Gunther 1998
Bando 1995
Hanley 1997
Crawford 2001
Schaffer 1999
Era of operation 1973-2004
74
76
78
80
82
84
86
88
90
92
94
96
98
00
02
04

Figure 6.8 – previous page. Histogram demonstrating the progressive reduction in operative mortality of atrioventricular septal defect with common atrioventricular junction, as reported in the literature

Risk factor for operative mortality	*Reference*
Pre-operative pulmonary hypertension	(Alexi-Meskishvili et. al., 1996; Boening et. al., 2002; McGrath et. al., 1987)
Pre-operative LAVV regurgitation, leaflet dysplasia or dysplastice LAVV	(Alexi-Meskishvili et. al., 1996; Chin et. al., 1982; Gunther et. al., 1998; Ross et. al., 1991; Tlaskal et. al., 1997)
Unbalanced ventricles	(Redmond et. al., 1996; Ross et. al., 1991; Schaffer et. al., 1999)
Double orifice LAVV or solitary papillary muscle	(Bando et. al., 1995; Chin et. al., 1982; Hanley et. al., 1993)
Additional ventricular septal defects	(Chin et. al., 1982)
Early era of operation	(Gunther et. al., 1998; Hanley et. al., 1993; Tweddell et. al., 1996)
Post-operative pulmonary hypertensive crisis	(Bando et. al., 1995)
Post-op LAVV regurgitation	(Bando et. al., 1995; Hanley et. al., 1993)
Young age at repair	(Studer et. al., 1982)(before 1976), (Gunther et. al., 1998) (before 1990), (Boening et. al., 2002)
Low body weight	(Boening et. al., 2002; McGrath et. al., 1987; Ross et. al., 1991)
Long aortic cross-clamp time	(Boening et. al., 2002; McGrath et. al., 1987)
Requirement for pre-operative inotropic support	(Alexi-Meskishvili et. al., 1996)
Requirement for pre-operative ventilatory support	(Alexi-Meskishvili et. al., 1997)
Non- closure of the Zone of apposition	(Boening et. al., 2002; Crawford, Jr. et. al., 2001)
Coarctation of the aorta	(Gunther et. al., 1998)

Table 6.4 This shows the risk factors for operative mortality identified by different groups in the literature. This contrasts to some of the findings made in the analysis of this data

Insights into valvar regurgitation

Post operative valvar regurgitation is an ongoing problem. Unlike the dramatic reduction of post-operative mortality, re-repair of the left atrioventricular valve remains at around 10% at 10 years in most series (Boening et. al., 2002). Early re-operation, which may be a technical problem with the repair, again remains stagnant at around 5-7% (Hanley et. al., 1993). Table 6.5 identifies some of the other risk factors identified by other groups over the years. In keeping with some of these findings, the most consistent risk factors identified, in both variants of atrioventricular septal defects were the absence of trisomy 21, and valvar dysplasia. The latter was independently associated with risk of re-operation in the absence of other variables. Trisomy 21 has been known for some time to confer a protective effect to the valve (Marino et. al., 1997). Little explanation of this has been given other than a possible increased expression of collagen VI during fetal development which may made the valvar tissue more robust (Gittenberger-de Groot et. al., 2003). In the study of Chapter 5, where the valvar tissue in atrioventricular septal defects was compared to the normal mitral valve, it was not possible to determine any differences between normal karyotype valves and the valves of those with trisomy 21 owing to problems collecting data. Whether alterations in molecular expression of collagen VI are translated to less dyspalsia of the subvalvar apparatus needs to be determined in future studies

Risk factor for post-op Left atrioventricular valvar regurgitation	Reference
Pre-operative LAVVR	(Fortuna et. al., 2004; Michielon et. al., 1995; Pozzi et. al., 1991)
Non-closure of the Zone of apposition	(Capouya et. al., 1992; Michielon et. al., 1995; Najm et. al., 1997; Ross et. al., 1991)
Absence of Trisomy 21	(Michielon et. al., 1997; Ross et. al., 1991)
Leaflet dysplasia	(Clapp et. al., 1987)
Double orifice left atrioventricular valve	(Clapp et. al., 1987; Fortuna et. al., 2004; Michielon et. al., 1995; Najm et. al., 1997)
Solitary papillary muscle arrangement	(Fortuna et. al., 2004)
Older age at operation	(Michielon et. al., 1997)
Division of the bridging leaflets at operation	(Fortuna et. al., 2004)
Earlier era of operation	(Crawford, Jr. et. al., 2001)
Unbalanced atrioventricular septal defects	(Clapp et. al., 1987; Ross et. al., 1991)
Pre-operative pulmonary hypertension	(Clapp et. al., 1987)

Table 6.5 The factors identified by varios groups as being significant for post-operative regurgitation of the left atrioventricular valve

Conclusions

Although the conclusions in this study of one institution's experience of the repair of atrioventricular septal defects are broadly in keeping with those of other groups when it comes to an analysis of post-operative mortality and re-repair of the left atrioventricular valve, it highlights an important problem. In the modern era of surgical repair exemplified by this cohort, mortality has fallen considerable to the point that the small numbers encountered may confound any analysis of risk factors. Since 2000, there have been no post-operative mortalities for the defect with the common orifice, and since 1994, there have been no deaths for the defect with a common orifice. This highlights the notion that operative success cannot be judged on the basis for this outcome. We are now looking at freedom for re-operation as being an important determinant for the quality of life, and hence ultimate success of the procedure.

Chapter 7: Conclusion, summary and further work

In this body of work, I have looked at the morphology of the left atrioventricular valve from a number of perspectives, in an attempt to bring its surgical repair into the modern era, in keeping with different aspects of its repair.

The advances made in the repair of the normal mitral valve have jumped leaps and bounds since the earliest days of cardiac surgery. Although the basic morphology of the mitral valve had been well known for many years prior to any attempts at repair, the eventual link between form and function was made by the surgeon's quest for a more perfect repair. Thus, in among the many accounts describing the results and experience of repair of the mitral valve, are many significant works delving into its applied morphology, and acting as guiding beacons along the way(Lam et. al., 1970a; Lam et. al., 1970b; Perloff et. al., 1972; Yacoub, 1976).

This philosophy, integrating and applying the morphology to the surgical issues must be made for the left atrioventricular valve in atrioventricular septal defects if the final aspiration of overcoming long-term valvar incompetence is to be met. Like with the case of the mitral, the surgeon must become the anatomist, using his knowledge of the morphology to define repair, all the while pushing the boundaries of surgical capabilities.

The first chapter set the scene and defined the problem in the historical context, emphasising that progress has been made to the point of considering this defect a so-called index lesion, where excellent results are expected from any unit attempting its repair.

The second chapter laid the groundwork for the subsequent chapters by providing a framework onto which to hang the concepts formed by later, more detailed analyses. Despite the obvious usefulness of analysing specimens to any

investigator looking into the morphology of any cardiac defect, the results of this flawed exercise should be interpreted with some caution. On the one hand, it provides the investigator with a unique perspective on the problem, with better access than any surgical incision. However, one may fail to realize that the specimens collected are often a very bias population, the morphology of which is skewed towards the more severe end of the scale. This is especially true for the more recent acquisitions in any collection; the so-called routine cases performed in this era, fortunately, never meet the pathologist's knife. My own qualitative and quantitative observations of the collections from London, Pittsburgh and Boston may certainly have been affected by this phenomenon, but where possible I had attempted to qualify my account with what had been observed in the operating room. Of course this was not possible in the instances where tendinous cords had to be counted, but until there is a way of doing this safely and quickly in the operating room, this flaw in the analysis will persist, and any such research will be sensitive to these criticisms.

In the third chapter, I re-visited the mitral valve and emphasised it as an example of the "ideal" atrioventricular arrangement, and one that the apparatus of the repaired left atrioventricular valve should aspire to. The arrangement of the subvalvar apparatus was emphasised allowing later comparisons to the repaired left atrioventricular valve. The main finding of this chapter was that the paediatric and adult valve were identical in their basic arrangement of the subvalvar apparatus. Furthermore, this highly conserved arrangement can be found in all normal hearts.

Given the strict morphologic principles seen in the mitral valve, especially at the commissures, indicates clearly that the zone of apposition between the bridging leaflets in atrioventricular septal defects cannot be described as the commissure of a tri-leaflet valve in the mitral sense, even after surgical attention.

The third chapter also highlighted that the morphologic arrangement of the valvar and subvalvar apparatus of the normal mitral valve is remarkably consistent, even at different stages of post-natal life. This stands in contrast to the variable morphology of the left atrioventricular valve in atrioventricular septal defects. This heterogeneity was explored further in Chapter 4, where it was shown that the morphology of the zone of apposition varied, depending on whether there was a common or separate atrioventricular valvar orifice. The defect with the separate orifices was often at the more severe end of the morphologic scale, but again, this may reflect the bias of the anatomic collections. It is well known that because of the cordal attachments to the crest of the ventricular septum, in atrioventricular septal defects, the ventricular septum acts as a papillary muscle. Beyond this, these septal cords may also form part of the coapting surface of the zone of apposition in the left atrioventricular valve. This may have implications for valvar competence if these cords are cut when trying to find space for the ventricular septal patch during repair.

Knowing what was gained about the morphology of the left atrioventricular valve and the mitral valve from the previous chapters, I moved to show that even after surgical repair, the left atrioventricular valve was not morphologically comparable to the "Gold Standard" set by the normal mitral valve. Thus, the repaired valve, is doomed to fail given the dysplasia of the subvalvar apparatus, and the manner in which the cordal mechanism after repair potentially places undue tension on the suture line at the leaflets. In other words, the mechanism of repair may produce a situation where the valve works against its own suture line, encouraging separation of the leaflets in the long term. It would be interesting to produce a laboratory model of this valve, in order to calculate the tensions across the suture lines using different modes of repair.

Ideally, it would also be important to see in there was any morphologic difference between the left atrioventricular valve in trisomy 21 compared to the normal karyotype. This was not possible given the paucity of data on the karyotypes of the samples, together with the limited population analysed, but this will have to be attempted in the future if we are to understand why the valve in trisomy 21 is more robust.

Finally, the morphology observed was placed in the context of the results of repair in the modern era, based on the surgical results at Great Ormond Street Hospital from 1994 to 2004. This not only confirmed the long-held belief that trisomy 21 confirms protection against post-operative valvar regurgitation, but that both valvar dysplasia and a dual orifice valve are risk factors for post-operative mortality and long-term regurgitation. As with the situation of specimen analysis, the small numbers of deaths prevented any meaningful conclusions from the statistics, and rather than hindering the contentions of this thesis, paradoxically serves to highlight the fact that in the modern era, mortality is so low that it is no longer the best outcome measure of success.

Future studies

The burning question that has been asked about the repair of the left atrioventricular valve, and which has been highlighted by this thesis is that of why the valve in Down's syndrome is more robust. This issue is now being addressed at the molecular level, where some have postulated that the greater expression of collagen VI in the endocardial cushions of hearts with trisomy 21 may account for the firmer valvar tissues (Gittenberger-de Groot et. al., 2003). Be that as it may, the impact of this altered expression on valvar and subvalvar dysplasia needs to be addressed. In

my study of the cordal divisions in normal and hearts with atrioventricular septal defects, it was not possible to conclude whether those hearts with trisomy 21 had a different degree of dysplasia at the subvalvar level. This was principally due to a combination of two factors, the limited numbers of specimens used, and the patchy karyotype data on the specimens. For this reason, the issue was not even approached during the study, although it has important implications for the understanding of long-term valvar competence.

Conclusions

Like in the case of the mitral valve, the only way that the final issue of valvar competence can be over come is by bridging form and function. Once the behaviour of the repaired valve is clarified by this approach, it will also permit investigations into the left atrioventricular valve to go beyond mere descriptive studies, and into the realms of prospective analyses such as with randomised trials. It is hoped that this thesis has defined the philosophy of approach for this issue to be taken further, in preparation for the next generation of patients who will be returning for reoperation in ever increasing numbers.

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